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THE LATE SIR PENDRILL CHARLES VARRIER-JONES.

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# EDITORIAL

## THE RIGID THORAX

THOSE accustomed to dealing with diseases of the respiratory tract are well aware of the dangers of a rigid thorax. It may profoundly influence prognosis and the choice of treatment, let alone the severity and duration of symptoms. Considering these responsibilities, the rigid thorax receives remarkably little discussion or comment: it is hardly mentioned in current textbooks or writings, and even more distant references are few and far between.

A rigid thorax may be defined as one in which a free respiratory excursion of the chest wall is absent, so that respiration is largely, if not entirely, diaphragmatic, even during forced breathing. This is the simplest definition, and it emphasises that the range of the subject extends far beyond those evident examples with permanent elevation and suspension of the thoracic cage in the inspiratory position. The latter is not an essential feature of a rigid thorax as it is commonly regarded, but is a concomitant frequently due to pathological changes in the lungs or pleura. This distinction is important, for its neglect implies that a rigid thorax is apt to be overlooked when abnormal elevation is not present also.

A primary grouping of examples of the rigid thorax divides them into those of functional and those of organic origin. There are subjects in whom a rigid thorax is unaccompanied by any discoverable signs of organic disease. Here the disability is usually betrayed in youth during some acute respiratory illness; or else it remains concealed until advanced years, when it may figure as a source of breathlessness on effort. Though it is important to exclude an organic cause for such rigidity, the distinction at this age matters less than in youth. The characteristics of this group, those with a functionally rigid thorax, are habitually defective breathing from choice rather than compulsion, often physical inferiority in other ways, an

asthenic build, sedentary occupation and habit, poor muscular tonus and training, and no relevant history or signs of pulmonary illness bearing upon the condition. The cause appears to be a neuromuscular defect of breathing, taking origin in faulty training or habitual avoidance of respiratory load. In this group the chest is usually fixed midway in a position between inspiration and expiration—though a few marked examples occur in young people, blameless as regards past illness, with a raised and rigid thorax held in a position of extreme inspiration, and unaccompanied by supporting signs of emphysema. Occupation is sometimes responsible for the elevation of the chest; but it is difficult to escape the conclusion that this arises often from overactivity of accessory muscles of inspiration due to reflex or other causes. This type of rigid thorax is less menacing than other forms, for it is generally less severe in its effects and is more amenable to treatment, at any rate in youth.

The rigid thorax due to organic disease is a potent source of disability. The usual form, with the chest fixed in extreme inspiration, is so often associated with fully fledged emphysema that the association has come almost to be regarded as invariable. But it occurs in other than emphysematous subjects, sometimes in a severe form. Here some other reason for permanent distension and fixation of the chest must be sought, though it often remains in doubt. Premature or excessive calcification of costal cartilages was held responsible at one time, but radiographs dispelled this explanation by failing to show any consistent relationship. Marked calcification, at any age, may be accompanied by a normal vital capacity and free movement of the chest wall. Gibbous and other deformities account for some obvious examples of the organic rigid thorax, just as spondylitis accounts for others. But then spinal as well as thoracic movements are restricted, pain becomes a feature, and there is scarcely need for radiological proof of the underlying cause. In others no evidence for spondylitis can be found, although it is tempting to regard it as the cause; some of these patients may have a limited arthritis of the costovertebral articulations, fixing the thorax, as Cecil Wall pointed out a few years ago. These subjects are usually elderly and fixation of the chest occurs in any respiratory position.

Another form of the rigid thorax is due to lesions in the upper dorsal or lower cervical spinal cord or in the intercostal nerves. Here the thoracic cage assumes a neutral position owing to the elastic recoil of the lungs, and there are also neurological signs in the foreground. This, the paralytic thorax, though immobile, is rigid in a functional sense only, as the efficient

modern treatment by mechanical respirators shows. Catatonic and stuporous subjects may show a similar inhibition of respiratory movement, at times dangerous to life.

Certain other factors may produce a rigid thorax, especially in older subjects. In many, who are not the victims of hypertrophic emphysema, age changes occurring in vessels and elastic tissue lead in time to a considerable loss of the power of distensibility of the lungs. There results what might be called a rigid lung, with fixation of the thorax as a secondary event. On clinical grounds it seems probable that senile emphysema thus plays a part in causing one type of rigid chest without distension of the lungs—a part as important in its way as that played by hypertrophic emphysema in leading to rigidity with distension of the lungs. Another factor, enfeeblement and disuse of intercostal muscles, has also to be considered in the elderly.

It is evident that much is yet obscure about the forms and causes of the rigid thorax. The emphysematous variety of the asthmatic or bronchitic subject, though numerically commonest, is not alone; and in so far as it has received an almost exclusive position in common regard, less obtrusive forms readily escape recognition.

Turning to the effects of a rigid thorax, the first is that it sets a limit to respiratory efficiency, and so becomes a potential or actual cause of shortness of breath. Apart from the contribution which it makes to the dyspnœa of asthmatic or chronic bronchitic patients, it is occasionally a sole cause for shortness of breath on effort with a reduced vital capacity. It may also add this symptom to the clinical picture during the course of toxæmic or febrile illnesses when otherwise it would not occur. These patients are often elderly, and on the strength of dyspnœa have usually been regarded as asthmatic or the victims of cardiovascular disease. A bout of acute bronchitis, or an abdominal catastrophe which throws diaphragmatic respiration out of action, may produce severe and increasing dyspnœa in these patients, due to the thoracic rigidity. It may even lead to a fatal outcome in what would otherwise have been no more than a temporary complication.

A second, and even more important, consequence of a rigid thorax is that it leads to ineffective cough. The mechanism of cough requires a full inspiration before an explosive effort can evacuate the bronchial tubes. Inability to make either a forced inspiratory effort or a forced expiratory effort is a direct cause of continued but useless coughing in patients with sputum. The ineffective cough disturbs rest and rapidly leads to physical

fatigue. Moreover, it also leads to the very real danger that accumulation of sputum will extend infection. This sequence of events is seen most often in elderly subjects with acute infections of the respiratory tract and also in phthisical subjects past middle life. It contributes in no small measure to rapid fatalities from "suffocative catarrh," and it is one reason why bronchitis so often becomes a chronic disease past middle life.

The most extreme examples of this effect of a rigid thorax are seen after abdominal operations, more particularly those with high incisions. Here the combined effects of the pain of the wound and of an abdominal binder so limit diaphragmatic respiration and the effectiveness of cough that literal suffocation is often the fate of these patients once a post-operative respiratory infection begins. No patient with a rigid thorax should readily undergo an abdominal operation if other treatment offers a reasonable prognosis. Beyond middle life, and with a background of respiratory infection, only operations required to preserve life are permissible. If possible abdominal operations should be done after preliminary rest and training with breathing exercises, when the respiratory tract is reasonably free from active infection and preferably during warm weather.

It is obvious enough that a rigid thorax affects prognosis in any malady where the efficiency of respiration is important. Acute infections of the respiratory tract, especially bronchitis, have their discomforts increased at the very least and past middle life their gravity as well; and the same applies in a protracted way to many chronic infections. In the tuberculous the rigid thorax influences treatment, and thus prognosis, in a special way, for it needs taking into account when deciding upon collapse therapy. No subject of a rigid thorax is a candidate of choice for an artificial pneumothorax, and much less for thoracoplasty. Moreover, it is a potent reason for refraining from the use of phrenic crush or evulsion.

Turning to consider treatment, improvement in the mobility of the chest wall and in the range of respiratory excursions can only be achieved with certain types of rigid thorax. In younger subjects who have no intrathoracic disease it often responds well to a prolonged course of physical training. Breathing exercises, though important for these patients, are only part of their physical treatment; the general physical debility which often goes with the thoracic defect calls for general exercises as well and the development of an interest in games or other sports. Some may also need psychiatric help beyond that which is transmitted by the confidence and skill of an instructor apt in breathing exercises.

For the bronchitic and asthmatic subject with a rigid thorax full training in the art of breathing is essential. The position of the thorax, the degree of emphysema and the severity of bronchial spasm decide how much of this training must be given to expiratory exercises; and the mobility of the thorax decides how much needs to be given to inspiratory exercises. Improvement depends very much upon the co-operation and intelligence of the patient, and upon facilities for proper training. Age is another factor in judging the degree of improvement likely to occur: only the young do really well.

For those whose rigid thorax is not associated with the common respiratory causes the value of breathing exercises is much less, though they should always be tried except in the old, or when severe deformity or spondylitis excludes hope of improvement. An important point is that diaphragmatic exercises are often wanted as well as costal. For the same reason obese subjects with a rigid thorax should lose weight and take exercise.

Breathing exercises before abdominal operations are already an established part of the routine of some surgeons, and they are essential for patients with fixed chests. They may often be started with advantage as soon as the decision to operate is made, and should be continued until chest expansion and vital capacity show improvement. These patients, like so many with respiratory infections, need also to be taught the technique of an effective cough. When a patient with a rigid thorax is actually dyspnœic at rest, he should be nursed sitting upright in bed, well supported with a fixed pillow at the knees, or else in a cardiac chair. Especially if there is cough, he needs a suitable bed table for the support of his shoulder girdle, which then allows more vigorous use of the accessory muscles of inspiration. These nursing points are, of course, well known, but it is not always sufficiently realised how important they are to the comfort and welfare of these patients. After abdominal operations, dressings should be retained in position with binders just tight enough for this purpose only, and not restricting breathing. When there is a rigid thorax the risk of a gaping wound is much less than the risk of suffocation.

Sufficient has been said to illustrate the importance of thoracic rigidity, and to show the limitations which it imposes upon its victims, and the difficulties of treatment. The special features of unilateral forms will be dealt with in a later editorial.

C. H.

# GENERAL ARTICLES

## GEORGE BODINGTON, 1799-1882

### THE PIONEER OF THE OPEN-AIR TREATMENT OF PULMONARY TUBERCULOSIS

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Dr. George Bodington, a member of an old Warwickshire family, was born in 1799 at Kenilworth Chase, and educated at Magdalen College School, Oxford.[1] An apprenticeship of five years' duration was then required of all candidates for an apothecary's licence,[2] and he served part of his apprenticeship at Atherstone, Warwickshire, and the remainder in London. He completed his professional education at St. Bartholomew's Hospital, and in 1825 obtained the diploma of Licentiate of the Society of Apothecaries.[3] He subsequently took the degree of M.D. at Erlangen University and the Licence of the Royal College of Physicians of Edinburgh.

He began his long professional career by engaging in general practice in Birmingham, but soon moved to Gravelly Hill, then a village, but now part of Birmingham. He married apparently while he was living at Gravelly Hill, his bride being a Miss Ann Fowler.

In 1836 he acquired a private lunatic asylum from two medical men named Terry and Horton, and became its resident medical superintendent.[4] This asylum, known as Driffold House, stood on elevated ground at Sutton Coldfield, about six miles from the centre of Birmingham. Sutton Coldfield, which is now continuous with and virtually a suburb of Birmingham, although it lies outside the city boundary, was then a small country town of about four thousand inhabitants.

When he began to treat pulmonary tuberculosis on open-air principles is not definitely known, but he was undoubtedly doing so in 1833. He was then living presumably at Gravelly Hill, and succeeded in arresting the disease in an awl-blade grinder. This patient, who was about thirty years old and had a cavity in one of his lungs, was treated in his own home, but Dr. Bodington ultimately came to the conclusion that the best results could be achieved only by his having his tuberculous patients under his own immediate

personal supervision, and on November 14, 1836, he received one, a woman aged 23, in his house. She was probably, but not necessarily, his first resident tuberculous patient. She went home in December, 1836, and was re-admitted during the following spring, 1837.[5]

Dr. Bodington's statement that this patient was placed under his roof[6] clearly implies that she stayed in the house in which he was actually living. The exact date on which he moved to Driffold House cannot now be ascertained, but he is definitely known to have lived there from 1836 until his retirement in 1868;[7] and Driffold House must, therefore, have been the one to which this patient was admitted during the spring of 1837, if not on November 14, 1836. But Driffold House was primarily an asylum, and a letter which he sent to the *Lancet* in 1841 affords conclusive evidence that he had received several insane patients during the preceding five years.[8] At least one case of tuberculosis, in addition to some cases of mental disease, must therefore have been admitted to Driffold House very soon after he had acquired it. This house thus appears to be the first one in which a resident patient, suffering from pulmonary tuberculosis, was treated on open-air principles, but since it served also as an asylum and hence fulfilled a double purpose, if only for a few months, it does not possess an unqualified claim to be regarded as the pioneer "sanatorium." This distinction without any reservation belongs to the White House, Maney, which was situated only a short distance from Driffold House. Dr. Bodington rented it a few years after he had acquired Driffold House, and used it for the treatment of tuberculosis.[9]

Several considerations may have prompted this step. Difficulties can hardly fail to have arisen from treating two entirely different kinds of patients on the same premises; and the prospect of living near to insane persons, in an institution that must have been well known locally as an asylum, would probably have deterred some prospective tuberculous patients from seeking admission. Moreover, Dr. Bodington hoped to extend the benefits of open-air treatment to more tuberculous patients, and he probably could not have received more than one or two at Driffold House without curtailing his asylum practice.

The White House was ready for the reception of, if not occupied by, patients, in January, 1840, when his epoch-making work on the open-air treatment of phthisis was issued in London by Messrs. Longman, Orme, Brown, Green and Longmans. It seems to have been his only published communication on the subject, and was entitled: *An Essay on the Treatment and Cure of Pulmonary Consumption on Principles Natural, Rational, and Successful.* The original edition is apparently very scarce,[10] but two reprints,[11] one with a portrait of Dr. Bodington and a facsimile of his signature,[12] were

published at the beginning of this century. A brief summary of the essay is appended.

Dr. Bodington's views on the ætiology of phthisis do not require detailed consideration. They were formed when the real cause of the disease was quite unknown, and came no nearer to the truth than those held by his contemporaries. It suffices to say that he believed that the presence of tubercles, acting as foreign bodies in the lungs, altered and weakened the influence exerted by the intra-pulmonary nerves, and, when this influence had been totally destroyed, the areas containing the tubercles began to break down. According to this theory, phthisis is in great measure a trophic disorder.

As regards treatment, the locality chosen should be high, free from fog and damp. A house in the country is to be preferred, for inland air is milder and therefore more suitable than sea-air.

The foundation of successful treatment is fresh air, " freely administered without fear." The air in the early morning is the best. Patients whose strength permits should walk about in the open for several hours a day, the duration being gradually increased; if too weak to walk for a sufficient length of time, they should ride on a horse or donkey, or take carriage exercise, with, in addition, as much walking as their condition warrants. A covered carriage with open windows may be used on wet days, but exercise in the open air must never be interrupted by adverse weather conditions. " The application of cold pure air to the interior surface of the lungs is the most powerful sedative that can be applied, and does more to promote the healing and closing of cavities and ulcers of the lungs than any other means that can be employed." Patients should always try to live in an atmosphere the temperature of which is the same as that of the outside air, and should avoid fires and hot, close rooms, and keep themselves warm by means of sufficient clothing.

A nutritious diet, consisting of plain animal and farinaceous food, should be taken in moderate amounts at frequent intervals. A glass of sherry, with an egg, may be given during the morning, and another after dinner.

A full dose of an anodyne, preferably morphine hydrochloride, should be administered at bedtime in order to prevent cough and secure a good night's rest. Much smaller, alterative doses, may be given during the day.

" In order effectually to overcome consumptive disease, all these several circumstances will be required to be adopted and followed up with the greatest attention, regularity, assiduity, and patience." Everything connected with the treatment should be strictly regulated by the practitioner, and he will secure the best results by having his patients under his personal

supervision in his own house. Some medical men should treat phthisis as a special branch of medicine; they should live in well-ventilated country houses, provided with all the necessary appliances, for the reception of patients referred to them by their colleagues in cities. Hospitals ought to be established in the vicinity of towns for the treatment of poor patients; some such provision is urgently needed for the Sheffield grinders, who, when cured or convalescent, "ought never to return to their former occupation, but should be employed after as agricultural labourers, gardeners, or in any other pursuit, rather than return to their former occupation."

The following extract from one of Dr. Bodington's case reports illustrates the kind of daily routine pursued by his patients:

"*August* 6, 1839.—Takes a glass of new milk before breakfast; rises at 6 a.m. and walks in the garden; breakfast, tea and toast; rides out afterwards; lunch, milk and toast; dinner, fresh meat and bread; three glasses of sherry wine daily, at 11 a.m., at 2 p.m., and at 7 p.m.; afternoon exercise in the open air, riding or walking; retires to bed at eight, takes an anodyne draught of mur. morphinæ; pulse 130."

This routine seems to have been fairly typical in all respects but one—the meagre diet. Either the patient was specially dieted, or Dr. Bodington's notes are incomplete, for he usually ordered much more generous living. The foodstuffs specifically mentioned in his *Essay* include fresh meat, pork-pie, gruel, boiled eggs, sago, bread, toast, and milk.

Treatment on the lines briefly described above was systematically carried out by Dr. Bodington's tuberculous patients, first at Driffold House, then, presumably, at the White House. It closely resembled what is nowadays termed "routine" sanatorium treatment, and differed from modern practice principally, but not exclusively, in the small part that was played in it by rest, to which Dr. Bodington seems to have attached relatively little importance. At the same time, he fully realised the necessity of an uninterrupted night's rest, and his description of one case shows that he ordered the patient, when at home, to sit about with the windows wide open, so that it is not impossible that his patients actually rested more than his *Essay* makes immediately apparent. Be that as it may, the advance that he made was truly immense. To modern readers his ideas are mere commonplaces; to his contemporaries they were revolutionary. The orthodox practice of the time demanded that patients should be confined to a closed room, sometimes kept constantly heated by a stove; their diet usually consisted of vegetables, rice and milk. In some cases emetics were given twice a week; in others frequently repeated small doses of tartar emetic, in order to induce diaphoresis and nausea rather than actual vomiting. So many different

drugs were supposed to be of value that it will suffice to mention that, in addition to tartar emetic, the ones most frequently ordered were digitalis, sodium carbonate, potassium nitrate, iodine, dilute hydrocyanic acid, and ipecacuanha. Amongst the other measures usually advised may be mentioned counter-irritants of various kinds, inhalations of diluted chlorine, residence in a mild climate, sailing, and exercise, preferably on horseback.[13]

An inevitable consequence of Dr. Bodington's method of treating phthisis and the success that he achieved by its means was his almost complete rejection of the orthodox teaching; and this he took not the slightest pains to conceal. It was probably his closely reasoned arguments against contemporary doctrine, rather than his actual methods, that led most of the medical journals to criticise his *Essay* most unsparingly. One review was favourable;[14] the others were uniformly hostile and derogatory.[15] The ultimate outcome can be described only as catastrophic. Dr. Bodington soon afterwards terminated his tenancy of the White House, and abandoned the open-air treatment of tuberculosis.

This step is said to have been the direct outcome of the adverse criticisms,[16] but whether it really was seems to be at least open to question. Dr. Bodington himself can scarcely have expected a warm welcome for a book that described a new method which differed radically from and was entirely opposed to contemporary theory and practice, and was from the pen of an obscure country practitioner. Furthermore, he was certain that he was in the right; and a man of his strength of character and convictions is not likely to have been unduly discouraged by the criticisms of persons whom he believed to be in the wrong. The deciding factor was probably lack of support from his colleagues, who failed to send him the cases which he had hoped they would send; but whether they allowed themselves to be swayed by the unfavourable criticisms in some of the medical journals, or whether these criticisms merely recorded their preformed opinions, must remain an open question.

Modern sanatorium treatment came after his death, and that it originated in his methods can hardly be supposed, since no definite continuity can apparently be traced between them. He worked alone, and he founded no school, and his *Essay* was forgotten or disregarded almost as soon as it was issued, until, in 1856, it was very favourably noticed in the *Journal of Public Health*.[17] Indeed, his work as regards tuberculosis seems to have been precursory rather than immediately effective and fruitful. But all this in no way detracts from the credit that is abundantly due to him. It is quite immaterial that his methods were based on a pathology that is now known to have been erroneous. What matters is that he anticipated modern sanatorium treatment when anything even remotely resembling

it was not only quite unknown, but at total variance with orthodox teaching. His methods were in some respects a combination of previous tendencies, but these were either so ill-defined or so little heeded by his contemporaries that none of the reviewers questioned his originality. Lastly, he had the courage of his convictions, and was not afraid to speak out plainly.

Little needs to be said of the remainder of his life. From 1843 onwards he confined his practice entirely to his insane patients at Driffold House, and was licensed for the reception of twenty.[18] He found time, however, to take a very active part in public life. He was a magistrate, and for many years a member of the Sutton Coldfield Corporation. This then consisted of a warden, who was elected annually, and twenty-four councillors, and he held the office of warden for two years (1852-1854). He was keenly interested in politics, and contributed many letters on this subject to the newspaper press.

He retired from practice in 1868, and his son, Dr. G. F. Bodington, succeeded him as Medical Superintendent of the asylum. He then moved to a house named "Rocksall," a few doors from Driffold House; it stood on the west side of the road now called Manor Drive, but is no longer in existence. He resigned his seat on the Sutton Coldfield Corporation in May, 1881, and, after a few months' illness, died at "Rocksall" on February 5, 1882, in his eighty-third year. He was buried in the graveyard of the Parish Church of The Holy Trinity at Sutton Coldfield, close to the boundary wall on the south side.

A bibliography of his writings will be found at the end of this article.

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Both Driffold House and the White House[19] are of such historical interest that no apology is required for including a brief account of them. Unfortunately, they do not seem to have been fully described in print when Dr. Bodington was treating cases of pulmonary tuberculosis in them, but at least a partial reconstruction of their general features is possible.

Driffold House was greatly enlarged and very much altered after Dr. Bodington had left it, and finally came to form part of a mansion called "The Driffold." In 1924 the present writer enjoyed the privilege not only of being shown "The Driffold" by its owner, the late Lieutenant-Colonel C. F. Fiddian-Green, but also of discussing with him the probable appearance of the entire property during Dr. Bodington's lifetime; and the following description is based principally upon the impressions that were then formed.

Driffold House in 1924 formed the central part of "The Driffold". It had originally been a three-storeyed, very substantially built, brick house, well set back from the road in an open and picturesque situation. With the

sole exception of the kitchen and some of the bedrooms, the interior had been altered and improved to such an extent that its appearance during Dr. Bodington's lifetime could not be satisfactorily determined.

Some outbuildings, which adjoined the road now called Wyndley Lane, stood near the house, and there could be no doubt of their being those which, according to an official report, had existed in 1862.[20] At the same time, there seems to be no reason to suppose that they were then of recent construction, and in all probability they existed when Dr. Bodington acquired Driffold House in 1836. In that case they presumably housed the carriages, horses, and a donkey which he used in the treatment of his tuberculous patients, and in 1924 they still contained the stables, which, however, had been much altered.

The land attached to Driffold House in 1859 measured sixteen acres, part of which was garden and part grassland, and Dr. Bodington owned also a farm of eighty-five acres in the vicinity.[21] The land attached to " The Driffold " in 1924 was not so large, but the approximate situation of the sixteen acres owned by Dr. Bodington could be inferred without risk of serious error. The greater part probably lay within the quadrilateral now formed by Driffold Road, Digby Road, Somerville Road, and Wyndley Lane; and the remainder lay in the direction of Wyndley Pool. As already mentioned, part of this land was a garden and part grassland, in 1858, and the garden could be readily identified. This garden, in which the tuberculous patients walked about, adjoined the south side of the house, extended in the direction of Digby Road, and was on level ground. The back of the house enjoyed uninterrupted views over Sutton Park, and the land there sloped downwards towards Somerville Road. This land must have been under grass during Dr. Bodington's occupation, but large parts of it had been levelled, and converted by Lieutenant-Colonel Fiddian-Green into ornamental terraces, gardens, and tennis courts. The farm of eighty-five acres, owned by Dr. Bodington, is known to have been somewhere in the vicinity; it probably lay in the direction of Wyndley Pool.

" The Driffold " has been pulled down. It stood on the west side of Driffold Road in the angle formed by the junction of that road and Wyndley Lane, and the approximate site of Driffold House is now occupied by two new houses named " Dunedin " and " Cedar Croft ". The whole of the land attached to Driffold House seems to have been built upon, and, so far as can be seen from the road, all the buildings formerly in Dr. Bodington's possession have been pulled down with the sole exception of the outbuildings. Parts of these are still standing; they adjoin and overlook the upper end of Wyndley Lane, near Driffold Road.

The White House, Maney, stood on the east side of the main road from

Birmingham to Sutton Coldfield, near the corner formed by the junction of that road with Holland Road. It lay within a few minutes' walk of Driffold House. The land that intervened between the two houses was probably quite open in Dr. Bodington's time; indeed, they may have been visible from each other; but this land is now built over and is intersected by the London, Midland and Scottish Railway line between Wylde Green and Sutton Coldfield Stations.

The White House was very much enlarged after Dr. Bodington had left it. Its size was at least doubled by building what was practically a new house onto the front of the original house. This addition greatly reduced the size of the front garden and had the effect of bringing the front of the White House into the centre of the enlarged building. This, in turn, received further additions, and the property was called " Maney House " in 1924, when the owner most kindly allowed the present writer to see it, and furnished him with many details of its history.

In spite of all the alterations that had taken place, the general features of the White House could be determined without difficulty. It appeared to have been a high, three-storeyed building, built of brick; and since it had been called the White House, had presumably been painted white outside. The staircase and landings were in the centre, and on each floor were two large rooms, occupying the ends, and extending through the entire depth, of the house. All these rooms in 1924 had windows opening onto the back garden; their front walls were partition walls, separating them from those parts of the premises that had been added to the front of the White House after Dr. Bodington had left it. Since it can scarcely be supposed that the front of the White House was entirely unprovided with windows, the conclusion is irresistible that every room had two windows, one in the front and the other in the back of the house, and therefore was excellently cross-ventilated. The ground floor contained one reception room, and the kitchen, scullery, etc.; the bedrooms, four in all, were on the first and second floors, and each bedroom would have provided ample accommodation for at least two patients. Some stables and outbuildings had stood near the house, but had been pulled down. A very large garden was attached to the house; part of it had apparently been a kitchen garden.

The writer has not been able to ascertain exactly when Dr. Bodington rented the White House, but it must have been in his occupation in January, 1840, when his *Essay* was published. As he himself stated in the introduction: " With the intention of further extending this mode of practice . . . I have taken for the purpose a house in every respect adapted, and near to my own residence, for the reception of patients of this class who may be desirous, or who are recommended, to remove from their

homes for the benefit of change of air, etc. It is presumed that, as the situation is very superior in point of dryness, mildness, and purity of air, the advantages to be derived from systematic arrangements with regard to exercise, diet, and general treatment, with the watchfulness daily—nay, almost hourly—over the patient of a medical superintendent, great advantages may be obtained by the consumptive patient treated in this way."

Dr. Bodington's statement that the White House was " in every respect adapted " for his purpose was no exaggeration. Indeed, the house could hardly have been improved upon at a time when modern sanatoria were quite unknown. During his tenancy the house was probably surrounded by open country, and the plan upon which it was constructed suggests that it may originally have been a dwelling-house attached to a farm. Tall, three-storeyed houses, built of brick, with two rooms on each floor, can still be seen on farms in Warwickshire, and probably elsewhere, and some of them seem to be practically identical with the White House, as it existed a century ago.

Dr. Bodington's tenancy of the White House cannot have lasted for more than a few years, but he undoubtedly received some tuberculous patients there,[22] and it is this fact that entitles the house to be regarded as the premier " sanatorium." According to the obituary notices in the medical journals, he confined his practice exclusively to his insane patients from the year 1843 onwards, and the Post Office Directory for 1845 gives his address as Driffold House only.[23] He seems, therefore, to have rented the White House for about three or four years. It was a girls' school in 1853.[24]

Maney House has been pulled down and the structural alterations in the immediate vicinity have been so extensive that its exact site is not easily determined. It must suffice to state that the White House stood approximately between the main road from Birmingham to Sutton Coldfield (near the Holland Road Corner) and the shops that adjoin the Odeon Cinema. These shops are well set back from the road, and the house seems to have stood in front of them. At least part of the garden appears to be included in the Odeon Cinema car park.

Several writers have stated that Dr. Bodington converted his institution for open-air treatment into an asylum. The writer has not succeeded in tracing this statement to its source, and is ignorant of the grounds on which it was originally made, but he nevertheless feels bound to mention that he is not aware of any evidence in favour of more than a very restricted conversion. The statement has, however, received such wide currency that brief recapitulation of the available data will not be out of place; and the writer will be greatly obliged to any of his readers who can shed any additional light on the matter.

The authors[25] of the obituary notices published in the medical journals after Dr. Bodington's death in 1882 made no mention of any conversion of the kind now under discussion, so that, if one had taken place, it cannot have reached their ears. Since these authors seem to have been well informed on all other matters relating to Dr. Bodington, it cannot have been well known when he died. Furthermore, Driffold House was an asylum when he acquired it in 1836. He undoubtedly received at least one resident tuberculous patient there in 1837 and probably did so in 1836, but he received also several insane patients from the year 1836 onwards, and there seems to be no evidence that the house ever entirely ceased to function as an asylum during the many years of his residence in it. Lastly, nothing has been found to suggest that insane patients were ever admitted to the White House, his tenancy of which cannot have lasted for more than a few years. So far, then, as the writer has been able to ascertain, if any conversion did take place it was only partial, and did not extend beyond restoring to their original use such parts of Driffold House as had been temporarily employed for the treatment of tuberculous patients.

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# THE PATHOGENESIS OF TUBERCULOSIS IN THE CALF

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## Introduction

Since the extensive experimental work of the Royal Commission on Tuberculosis (1904-9) there have been few contributions to the subject of natural and experimental tuberculosis in the calf published in Great Britain. A great deal has been published on the Continent, mainly in Germany, and this for the most part emphasises the importance in young calves of primary tuberculosis of the intestines and mesenteric lymph nodes. The lesions in the former site are usually small and only found on careful examination: the mesenteric nodes are always involved macroscopically and generalisation to other sites, especially the lungs, is common. Primary tuberculosis of the lung in the calf is considered by most of the German workers to be due to aspiration of infected material—either milk from cows with tuberculous mastitis or sputum from cattle with "open" pulmonary tuberculosis.

In contrast to this view, Calmette and his school have always maintained that a high proportion of cases of primary lung tuberculosis in man and animals is the result of alimentary infection in which the tubercle bacilli penetrate the intestine and pass through the mesenteric nodes without leaving any evidence of tuberculosis and finally produce lung lesions. The bacilli are also considered able to exist for considerable periods in the lymph nodes—so-called "latent" tuberculosis. Some observations recently reported by Edwards (1937) on tuberculosis in calves produced by feeding raw milk appear to support this view, since macroscopic tuberculous lesions were confined to the lungs and bronchial and mediastinal lymph nodes.

The experiments described in this paper, carried out in 1938-39, were designed to study the pathogenesis of tuberculosis in young calves infected with tubercle bacilli in varying doses and by different routes. Attempts were made to limit as far as possible the portal of entry to one site and to study the development of the lesions under conditions more standardised than those possible during an ordinary feeding experiment.

## Methods

Twenty-four animals were used, these being bull calves obtained from a tuberculin-tested herd. They were received at the Institute when five to

seven days old, having received an adequate supply of colostrum on the farm. They were housed in separate pens and were bedded on straw from a tuberculosis-free farm, and hay from the same source was later given to the calves *ad lib*. During the first three weeks the animals were fed on pasteurised milk or, in later experiments, on a proprietary " milk substitute." Cod-liver oil of guaranteed vitamin content was supplied, but conditions in the heart of London precluded access to sunlight or grass.

The animals were weighed on arrival and at weekly intervals during the course of the experiments. Animals which did not die naturally were killed with a captive bolt humane killer. Details of the individual experiments are given in the text, but the following was the routine autopsy procedure: calves destroyed with the humane killer were examined within a few minutes of death and in other cases after as short an interval as possible. A detailed autopsy was made, special attention being paid to the intestines, which were opened throughout their entire length and examined from the mucous and serous aspects with especial reference to the lymphoid tissue. Naked-eye lesions of tuberculosis were examined microscopically for tubercle bacilli and if positive no guinea-pig inoculations were carried out. In other cases guinea-pigs were inoculated with material, untreated as well as after treatment with antiformin. In most animals showing no naked-eye lesions a series of organs and glands was similarly treated, the tissues usually selected being tonsil and pharyngeal, hepatic, mediastinal, bronchial and mesenteric lymph nodes and, in some cases, the spleen. Material from most of the organs and lymph nodes was fixed in formol saline, and histological sections were prepared and stained with hæmatoxylin and eosin and by the method of Ziehl-Neelsen. Guinea-pigs which failed to die of tuberculosis or showed no ulcerating local lesion were killed and examined five months after inoculation.

### 1938 Experiments. Milk, Slightly or Heavily Contaminated with Tubercle Bacilli, fed by Bucket or by Stomach Tube

Four pairs of calves were used for these experiments, the animals being fed morning and evening. Two pairs received 14 daily doses of ordinary raw bulk milk, which constantly contained small numbers of tubercle bacilli sufficient to infect guinea-pigs, though not usually demonstrable in smears of centrifuged deposit. The infectivity of the milk for guinea-pigs was confirmed for the particular samples of raw milk employed. The other calves received three doses of half a pint of heavily contaminated milk obtained by mixing several samples from cows with tuberculous mastitis. This milk infected guinea-pigs in a dilution of 1 : 100,000 and tubercle

bacilli were readily demonstrable in smears of the deposit. It was diluted 1 : 4 with pasteurised milk before being fed to the calves, whilst the ordinary raw milk was fed undiluted.

In each group of four animals one pair drank the contaminated milk out of an ordinary bucket, while the other pair were given it by stomach tube passed into the rumen. It was hoped that by using a stomach tube it would be possible to avoid regurgitation with consequent soiling of the pharynx. Pasteurised milk was given at the other daily feed, and this was administered by the alternative method in such a way that all the animals were fed by both methods daily—*e.g.*, calf 1 got the raw milk from a bucket in the evening and pasteurised milk by tube in the morning, calf 3 got the raw milk by tube in the morning and pasteurised milk from a bucket in the evening. No difficulty was experienced in passing the stomach tube. although in spite of very slow and careful administration of the milk two calves (Nos. 4 and 8) were seen to regurgitate during feeding. During withdrawal of the tube pasteurised milk was run through so as to minimise the risk of carrying infected milk into the throat. The total amount of slightly contaminated (raw) milk given to each calf was about 30 pints. Since 0·1 c.c. of this milk produced tuberculosis in a guinea-pig, this amount must have contained at least one tubercle bacillus, so that the total dose must have been at least $10 \times 500 \times 30$—*i.e.*, 150,000 bacilli. The amount of the highly contaminated milk received by each of the four calves was $1\frac{1}{2}$ pints, of which 0·1 c.c. was capable of infecting a guinea-pig when diluted 1 : 100,000, so that the least number of tubercle bacilli contained in the total dose would have been $10 \times 100{,}000 \times 750$—*i.e.*, 750 million organisms. The total numbers of bacilli given to the two series of calves were thus in a ratio of about 1 : 5,000.

Results. (*a*) *Calves given Ordinary Raw Milk.*—Two of these failed to develop tuberculosis, viz., one which received the contaminated milk by tube (calf 3) and the other by bucket (calf 1). Three of the four animals showed a normal weight curve; the fourth (calf 4) regurgitated and aspirated some of the contaminated milk and recovered only after several days' severe respiratory distress. The two infected calves gave a strongly positive intradermal reaction following a single injection of tuberculin, the skin measurements attaining 20 to 30 mm. and the swelling being diffuse and œdematous. Both animals showed at autopsy primary lung tuberculosis of the aspiration type with caseous bronchial nodes and involvement of the anterior mediastinal nodes. It is reasonable to assume that the infection was by aspiration and that this type of lesion may follow bucket feeding with milk contaminated with tubercle bacilli. An infective dose which was sufficient to cause aspiration tuberculosis in the lungs was apparently too

small to cause intestinal or mesenteric node lesions, both histological examination and guinea-pig inoculation being negative. There was no evidence that the lung lesions were secondary to absorption of the bacilli from the intestine without provoking a reaction and their subsequent passage to the lungs.

(*b*) *Calves given Highly Contaminated Milk.*—All these failed to gain weight normally. Calf 7 was killed *in extremis* twenty-seven days after the last feed; on autopsy no tuberculous lesions were detected but both kidneys were the seat of an acute focal interstitial nephritis. The remaining three (Nos. 5, 6 and 8) gave positive reactions to the tuberculin test. Calf 5 showed at autopsy primary tuberculosis of the tonsil and intestine, lesions being present at the site of entry and regional lymph node in each case. In calf 6 there was primary tuberculosis of the lung and bronchial node and a second primary lesion in the right suprapharyngeal node. The tonsil was positive on guinea-pig inoculation. Calf 8 was the one which regurgitated and showed at autopsy primary tuberculosis of the lung and bronchial node. The anterior mediastinal node was caseous and there was also a calcified lesion in a mesenteric node. The tonsil and suprapharyngeal node were positive on guinea-pig inoculation. The experimental results are summarised in Table I.

*Conclusions.*—These preliminary experiments suggested that a small dose might produce primary tuberculosis of the lungs by aspiration but fail to cause lesions in the intestine or mesenteric nodes. Large doses appear to facilitate alimentary infections in the throat or intestine or in both sites, with or without respiratory infection. Multiple primary infection may then occur. The experiments with the stomach tube were inconclusive owing to regurgitation, and further experiments were therefore devised in which the portal of entry could be limited to the intestine without the risk of regurgitation.

### 1939 Experiments

In view of the unsatisfactory results obtained by the use of a stomach tube it was decided to introduce a culture of bovine tubercle bacilli directly into the duodenum of calves under general anæsthesia. A virulent culture of bovine tubercle bacilli, grown on Dorset's egg medium for about four weeks, was used. Preliminary experiments were carried out on two calves, but the animals died as a result of the anæsthetic. The anæsthetic first tried was nembutal intravenously, which was known to be very suitable for producing general anæsthesia in dogs and swine. The results with calves, however, were unsatisfactory, one calf failing to recover from the anæsthetic (calf 10) and the other (calf 9) dying of a hypostatic gangrenous pneumonia.

TABLE I
PRELIMINARY EXPERIMENTS

**TABLE I**
**PRELIMINARY EXPERIMENTS**

| *Calf No.* | *Method of Administration* | *Dose.* | *Clinical History.* | *Time in Days until Autopsy.* | *Findings at Autopsy.* | *Guinea-pig Inoculation.* | *Conclusions.* |
|---|---|---|---|---|---|---|---|
| 1 | Raw bulk milk p.m. by bucket; pasteurised milk a.m. by stomach tube | 14 daily doses of raw bulk milk (30 pints in all) | Good weight increase. Tub. test neg. 71 days after 1st dose | 74 | No tuberculosis | Tonsil and node neg. Mediastinal node neg. Mesenteric node neg. | No tuberculosis. |
| 2 | Ditto | Ditto | Good weight increase. Tub. test pos. 56 days after 1st dose | 59 | Bronchial and med. nodes caseous. Caseous broncho-pneumonia. Early calcification in sections of all lesions | Tonsil and node neg. Mesenteric node neg. | Primary aspiration tuberculosis→mediastinal node. |
| 3 | Raw bulk milk a.m. by stomach tube; pasteurised milk p.m. by bucket | Ditto | Good weight increase. Tub. test neg. 71 days after 1st dose | 74 | No tuberculosis | Tonsil and node neg. Bronchial node neg. Mesenteric node neg. | No tuberculosis. |
| 4 | Ditto | Ditto | Regurgitated and aspirated at a morning feed; recovered. Tub. test pos. 56 days after 1st dose | 59 | Bronchial and med. nodes caseous. Caseous broncho-pneumonia. Early calcification in sections of lung and bronchial node lesions | Tonsil and node neg. Mesenteric node neg. | Primary aspiration tuberculosis→mediastinal node. |
| 5 | Pasteurised milk a.m. by stomach tube. Tuberculous mastitis milk p.m. by bucket | 3 daily doses of ½ pint heavily contaminated milk | Fair weight increase. Tub. test pos. 49 days after 1st dose | 52 | L. phar. and submax. nodes caseous. Caseous foci in two mesenteric nodes and in one Peyer's patch. Microscopic tub. left tonsil. Calcification in lymph nodes | Bronchial node neg. Mediastinal node neg. | Primary tuberculosis of tonsil and intestine. |
| 6 | Ditto | Ditto | Slight weight increase. Tub. test pos. 25 days after 1st dose | 27 | Caseous tuberculosis of lungs and br. and med. nodes. Micro. lesion in left phar. node | Tonsil and node pos. Mesenteric node neg. | Primary aspiration tuberculosis and throat infection→mediastinal node. |
| 7 | Tuberculous mastitis milk a.m. by stomach tube. Pasteurised milk p.m. by bucket | Ditto | Failed to gain weight. Tub. test doubtful reaction 25 days after 1st dose | 27 | No tuberculosis. Focal interstitial nephritis | Tonsil and node neg. Mesenteric node neg. | No tuberculosis. Nephritis. |
| 8 | Ditto | Ditto | Regurgitated at a morning feed. Tub. test pos. 49 days after 1st dose | 52 | Caseous broncho-pneumonia. Caseation bronchial, med. and mesenteric nodes. Micro. calcification in lymph node lesions | Tonsil pos. Pharyngeal node pos. | Primary aspiration tuberculosis and throat and intestinal infection. |

Subsequently, pentothal sodium was used intravenously; this gave a period of anæsthesia lasting some twenty minutes, which was quite long enough for our purpose. In the first trials the culture was injected into the duodenum at a point about 10 cm. from the pylorus with a syringe which was rinsed with sterile saline before and after the injection. This resulted in the formation of a tuberculous nodule in the wall of the duodenum (calf 9) and was clearly unsatisfactory. In further experiments the culture suspension was enclosed in a gelatin capsule of the type used for measured amounts of solid drugs, the capsule being immersed subsequently in collodion to ensure perfect sealing. The animal was tied on a table in the dorsal position, the anæsthetic was injected, an incision about three inches long made in the abdominal wall from the xiphoid cartilage backwards and the abomasum and duodenum exposed. The wall of the abomasum was then incised, an ejector carrying the capsule was inserted through the wound into the duodenum and the capsule liberated. The abomasal incision was closed, the abdominal wound sutured and adhesive bandages passed round the body. In this way no lesion resulted in the duodenal wall, but subsequent experience showed that some of the capsules had leaked with resulting tuberculosis of the abomasal wall and covering peritoneum.

Calf 11 was given in this way 0·01 mg. of culture; it remained in good condition and showed no lesions of tuberculosis when killed thirty-six days later. Calf 12 was given 1·0 mg. of culture and failed to gain weight at the normal rate. It was killed seventeen days after the operation and showed tuberculosis of the abomasal wound and of the regional (abomasal) lymph node. Histological examination showed small foci of epithelioid cells in the hepatic and in two mesenteric lymph nodes. In addition the mediastinal node was infective for guinea-pigs.

A series of six calves (Nos. 13 to 18) was then given varying doses of tubercle bacilli in *double* gelatin capsules, a small capsule containing the culture being enclosed immediately within a larger capsule and the latter sealed by dipping several times in collodion.

Results.—Calves 13 and 14 received 1·0 mg. of culture. Calf 13 died thirty-six hours after the operation from an acute streptococcal infection. Calf 14 did well and gave a positive reaction to an intradermal tuberculin test fifty-six days after the operation. At autopsy, carried out two days after the test, there was extensive tuberculosis of Peyer's patches throughout the small intestine, with caseation and calcification. Caseous lesions were also present in the mediastinal, hepatic and bronchial nodes, and there was generalisation involving the lungs and spleen. In this calf the abomasal wound also showed tuberculous foci, the gelatin capsule having come apart during insertion.

Calves 15 and 16 received 10·0 mg. by the same method, but in both animals the capsule had probably been accidentally liberated from the ejector in the abomasum. Calf 15 failed to gain weight normally and was killed thirty-six days after operation. At autopsy there were primary caseous lesions in all the mesenteric nodes and Peyer's patches. The lesions in the former showed calcification in sections. The hepatic node showed epithelioid cell tubercles histologically. The cardiac lobes of both lungs were consolidated, with abscess formation, and *C. pyogenes* was isolated from the lesions. One guinea-pig receiving a suspension prepared from the bronchial lymph node developed a lesion in the regional lymph node. This was inoculated into a second guinea-pig, producing typical tuberculous lesions. Calf 16 also failed to thrive and was found dead fourteen days after the operation. There was no macroscopic evidence of tuberculosis, although the granulation tissue at the operation site in the abomasum showed numerous acid-fast bacilli and a few lesions of productive type were found in the mediastinal lymph node. On guinea-pig inoculation, the pharyngeal, bronchial, hepatic and mesenteric nodes were all positive for tuberculosis. (This may perhaps be explained by generalisation of the disease *in extremis*.)

Calves 17 and 18 were given 80·0 mg. of culture in a double capsule into the duodenum and were killed after twenty-three and fifty-four days respectively. Calf 17 was in poor condition and showed caseous Peyer's patches and mesenteric nodes. The abomasal wound was free from tuberculosis on histological examination. The mediastinal and hepatic lymph nodes were positive for tubercle bacilli on guinea-pig inoculation; the bronchial and pharyngeal nodes and the spleen gave negative results. Calf 18 was in good condition when killed; the mesenteric nodes were caseous and showed macroscopic calcification. The Peyer's patches were caseous and ulcerating. Small foci of caseation and calcification were seen histologically in sections of the abomasal wound. The tonsil and pharyngeal, bronchial, mediastinal and hepatic nodes were negative on guinea-pig inoculation.

In view of the common use of the teat bucket in commercial calf-rearing three calves were given varying doses of culture in a pint of milk by this method. Calf 19 was given 1·0 mg. of culture and reacted to a tuberculin test twenty days later. When killed at twenty-three days the mesenteric nodes were slightly enlarged and contained a few minute greyish foci. Three minute foci were also found on careful examination of the opened small intestine, each being situated in a Peyer's patch. Several acid-fast bacilli were seen in smears of these intestinal lesions. The tuberculous nature of the lesions in both mesenteric nodes and Peyer's patches was

confirmed histologically, these being foci of epithelioid cells containing a fair number of acid-fast bacilli. The spleen, pharyngeal node and tonsil, and the bronchial and hepatic nodes were negative on guinea-pig inoculation, while the mediastinal node was positive.

Calf 20 received 0·01 mg. of culture by teat bucket and was negative to the tuberculin test fifty-six days later. The carcase of this animal was in poor condition, with considerable anasarca when the animal was killed fifty-nine days after administration of the dose. The only macroscopic evidence of tuberculosis was a small caseous focus in one mesenteric node which was found when the node was cut for embedding in paraffin. In histological section this lesion showed calcification, and several epithelioid cell foci were also found in other mesenteric nodes. The pharyngeal node and tonsil, bronchial and hepatic nodes and spleen were negative on guinea-pig inoculation; the mesenteric nodes — inoculated before the macroscopic lesion referred to was discovered—were positive.

Calf 21 received 0·0001 mg. and reacted to the tuberculin test after fifty-six days. Two days later the animal was killed. The right bronchial lymph node was caseous and smears showed a considerable number of acid-fast bacilli; the left bronchial node was slightly enlarged. Histological examination showed epithelioid cell foci in the mediastinal node. The lungs were free from tuberculosis. The tonsil and pharyngeal node, spleen, hepatic and mesenteric nodes failed to produce tuberculosis on inoculation of guinea-pigs.

From the results obtained by Wilson and Schwabacher (1937) it may be assumed that 1 mg. of moist culture would contain a minimum of 1,000 million tubercle bacilli of which at least 10 per cent. are viable. The number of viable organisms given to calves 19 and 21 would thus be 100 million and 100 thousand respectively, and therefore of the same order as the dose given in the form of naturally contaminated milk to calves 5-8 and 1-4 respectively.

In an attempt to confirm the results of previous workers, three calves were inoculated intratracheally with culture. The inoculation was made in the mid-ventral line in the lower third of the neck. A fairly long needle of wide bore was used and steps taken to ensure that the point of the needle was actually within the tracheal lumen. The dose of culture was given in 1·0 c.c. of saline and no coughing resulted. Calf 22 received 1·0 mg. by this method. The animal reacted to a tuberculin test twenty-two days later and was killed at twenty-four days. The only signs of tuberculosis at autopsy consisted of a caseous nodule in the trachea at the site of injection and caseation in the local (middle cervical) lymph nodes. The tracheal nodule showed enormous numbers of tubercle bacilli on section and there

was early calcification. There were small epithelioid cell foci in the bronchial, mediastinal and pharyngeal lymph nodes; these lymph nodes together with the hepatic node were all positive on guinea-pig inoculation, while a mesenteric node was negative. Calf 23 received 0·01 mg. by the same route; it became extremely weak and had severe and persistent diarrhœa, dying forty-one days after injection. There was a local caseous lesion at the site of injection and caseation of the regional lymph nodes. The mediastinal node showed small epithelioid cell foci on section. The lungs showed a pneumonia due to *C. pyogenes*. The mediastinal and bronchial nodes were positive, the mesenteric nodes and pharyngeal nodes and tonsil were negative when inoculated into guinea-pigs. Calf 24 received 0·0001 mg. intratracheally. It also became very weak, lost weight and had profuse diarrhœa. It died thirty-one days after inoculation. There was no macroscopic tracheal lesion, but the cervical lymph nodes near the injection site were caseous. The mediastinal node showed proliferation of sinus endothelial cells on section, but no acid-fast organisms were seen.

Table II. gives a summary of the most important findings.

**Discussion and Literature**

It is not proposed to discuss in detail the literature dealing with tuberculosis in bovines published prior to 1910, as this has been reviewed by M'Fadyean (1910). He criticised in particular the experiments of Calmette (1905, 1906), which purported to show that tubercle bacilli administered to goats by stomach tube were able to produce macroscopic lung lesions without evoking a recognisable reaction in the mesenteric nodes. A careful examination of Calmette's papers shows that the experiments do not prove this, but merely show what was already well known—that primary alimentary infection may set up secondary lung lesions. M'Fadyean, in the same paper, describes in some detail the experiments, carried out by the Royal Commission, on the feeding of calves with tubercle bacilli either in the form of culture or by sucking a cow with tuberculous mastitis. The most important conclusion reached was that " in the case of cattle the almost invariable result of infection by ingestion is a tuberculosis with more or less conspicuous lesions in the abdominal cavity, and especially in the mesenteric gland " (p. 250). It was found difficult to set up a progressive, rapidly fatal infection, even in young calves and using relatively large doses of bacilli; *e.g.*, $10 \times 10^6$ bacilli produced lesions confined to the intestine and mesenteric nodes in three calves killed thirty-five to forty-four days after receiving the dose *per os*. In several calves there were tuberculous lesions in the tonsils or pharyngeal nodes, suggesting the pharynx as the

## TABLE II

### 1939 EXPERIMENTS

| *Calf No.* | *Method of Administration.* | *Dose in Mg.* | *Clinical History.* | *Time in Days between Dose and Autopsy.* | *Findings at Autopsy.* | *Guinea-pig Inoculation.* | *Conclusions.* |
|---|---|---|---|---|---|---|---|
| 9 | Culture injected into duodenum under nembutal anæsthesia | 10 | Anæsthesia lasted 48 hours; pneumonia developed. Destroyed | 6 | Gangrenous pneumonia and pleurisy. Enormous number of tubercle bacilli at injection site | None | Anæsthetic pneumonia. Local tuberculous lesion. |
| 10 | Ditto | 1 | Failed to recover from anæsthetic | 1 | None | None | Death under anæsthetic. |
| 11 | Capsule inserted into duodenum through abomasal incision under pentothal sodium anæsthesia | 0·01 | Good weight increase | 36 | No macroscopic tuberculosis | None | No macroscopic tuberculosis. |
| 12 | Ditto | 1 | Slight weight increase | 17 | Early tuberculosis of abomasal wound and of gastric, hepatic and two mesenteric nodes | Mesenteric and med. node pos. Bronchial, pharyngeal and colic nodes neg. | Primary tub. at operation site and in mes. node → mediastinal node. |
| 13 | Double capsule used | 1 | Died 36 hours after operation | 1½ | Umbilical abscess and signs of septicæmia | None | Post-operative death. |
| 14 | Double capsule used. (Lid of capsule came off in abomasum) | 1 | Good weight increase. Tuberculin test pos. 56 days after operation | 58 | Caseous abomasal wound; all Peyer's patches caseous. Caseation and calc. mes. nodes. Miliary tub. lungs. Caseous bronchial, med. and hepatic nodes. Tubercles histologically in spleen | Tonsil and phar. node neg. | Primary alim. tub. → mesent. nodes→generalisation. |
| 15 | Double capsule used. (Capsule probably freed in abomasum) | 10 | Poor weight increase | 36 | Caseous Peyer's patches and mes. nodes. Histological tub. in hepatic node. Abscesses in lungs due to *Corynebacterium pyogenes* | Tonsil and phar. node neg. Spleen neg. Bronchial node pos. | Primary alim. tub. → hepatic and mesenteric nodes. |
| 16 | Ditto | 10 | Became very weak; | 14 | No macroscopic tuberculosis. | Bronchial, pharyn- | Primary abo- |

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|---|---|---|---|---|---|---|---|
| 16 | Ditto | 10 | Became very weak; died | 14 | No macroscopic tuberculosis. Early lesion in sections of abomasal wall and mediastinal node | Bronchial, pharyngeal, hepatic and mesenteric nodes all positive | Primary abomasal lesion → med. node. Generalisation. |
| 17 | Double capsule successfully introduced into duodenum | 80 | Poor weight increase; diarrhœa | 23 | Caseous foci in Peyer's patches and mesenteric nodes. Abomasal wound free from tuberculosis | Med. and hepatic nodes pos. Bronchial and phar. nodes and spleen neg. | Primary alim. tub. → mesenteric and hepatic nodes → mediastinal node. |
| 18 | Ditto | 80 | Good weight increase. Tuberculin test pos. 52 days after operation | 54 | Peyer's patches caseous; mes. nodes caseous and calcified; hepatic node caseous. Tuberculosis of abomasal wound in section, with calcification | Tonsil and phar. node, bronchial and mediastinal nodes and spleen all negative | Primary alim. tub. → hepatic and mesenteric nodes. |
| 19 | Culture given in milk by teat bucket | 1 | Tuberculin test pos. 20 days after dose | 23 | Minute caseous foci in three Peyer's patches. Tuberculosis in sections of mesenteric nodes | Tonsil and phar. node, bronchial and hep. nodes neg. Mediast. node pos. | Primary alim. tub. → mesent. node → mediast. node. |
| 20 | Ditto | 0·01 | Tuberculin test neg. 56 days after dose | 59 | Minute caseous focus in 1 mes. node; calcification in sections | Tonsil and phar. node, hep. and bronch. nodes and spleen all neg. Mesenteric node positive | Primary alim. tuberculosis → mes. node. |
| 21 | Ditto | 0·0001 | Tuberculin test pos. 56 days after dose | 58 | Right bronchial node caseous. Histological tuberculosis in mediast. node | Tonsil and phar. node, hepatic and mesenteric nodes and spleen all neg. | Primary resp.-tuberculosis → bronchial node → mediast. node |
| 22 | Intratracheal injection of culture | 1 | Tuberculin test pos. 22 days after injection | 24 | Local caseous tracheal lesion and caseous local cervical node. Early tub. lesions in sections of phar., bronchial and mediastinal nodes | Tonsil and phar. node, bronchial, mediast. and hepatic nodes pos. Mes. nodes neg. | Primary tub. trachea, throat and intestine (hep. node) → mediast. node. |
| 23 | Ditto | 0·01 | Became very weak; died | 41 | Local caseous tracheal lesion and caseous local cervical node. Suppurative pneumonia (*Corynebacterium pyogenes*). Early tub. in sections of mediastinal node | Tonsil and phar. node and mes. node negative. Bronchial and mediast. nodes positive | Primary tracheal tub. → local node → bronchial node → med. node. |
| 24 | Ditto | 0·0001 | Ditto | 31 | Caseous lesion in local cervical nodes | None | Tuberculosis of regional node. |

portal of entry. Lesions in the hepatic nodes often accompanied mesenteric node involvement, and this is in agreement with our own findings. The portal or hepatic nodes drain lymph from the duodenum as well as from the liver, pancreas and the gastric nodes (Sisson, 1938; Ellenberger and Baum, 1926).

M'Fadyean summarises the very considerable amount of evidence in favour of the greater ease of infection by inhalation than by ingestion. He refers to experimental work carried out by various workers (Reichenbach, Findel, Alexander, Kossel *et alia*, Weber and Titze, etc.). Using guinea-pigs, rabbits and calves, Weber and Titze found 10·0 mg. to be the minimal dose needed to infect calves by ingestion, whereas 0·01 mg. was sufficient by inhalation. In the guinea-pig Findel calculated that 62 tubercle bacilli constituted an invariably infective dose by inhalation; no infection, however, developed when 19,000-382,000 bacilli were given in the food. The infective dose by ingestion was estimated to be at least ×19,000 that by inhalation.

The conclusion drawn by M'Fadyean from this review of the literature and from his own work, including the experience of the Royal Commission, was that inhalation is probably the commonest natural method of infection in cattle. Natural cases should be ascribed to ingestion only when the lesions found at autopsy are confined to the abdomen or when the abdominal lesions are older than those elsewhere.

Chaussé (1911) carried out ingestion and inhalation studies in sheep and cattle; he found it possible to infect both species very readily by inhalation of air containing tubercle bacilli in suspension. Calves developed pulmonary lesions after a single exposure to air containing 0·125 mg. of culture, whereas 100·0 mg. given by stomach tube was insufficient to cause infection.

Rautmann (1935) infected four calves, five to six months old, by a single large dose (4·5 to 6 litres, given by stomach tube) of milk from a cow with tuberculous mastitis. The milk was rich in bacilli, there being organisms in every field under the oil immersion objective. One calf regurgitated, due probably to stimulation of antiperistalsis by the passage of the stomach tube. The animals were all negative to tuberculin prior to the experiment; three of the four reacted when re-tested three weeks after receiving the infective dose. The calves were killed at four, seven, thirteen and twenty weeks. All four showed primary tuberculosis of the mesenteric nodes, with intestinal lesions in addition in two animals. Generalisation had occurred in the animal killed after twenty weeks. The portal lymph nodes contained tubercle bacilli in two calves and the pharyngeal and submaxillary nodes were involved in one.

The time required for the development of microscopically recognisable calcification in young calves is given by Hildenbrand (1936) as three weeks after infection; the same author states that at least fifty days must elapse before macroscopic evidence of calcification (*Verkreidung*) is seen.

Perhaps the most extensive experiment on the pathogenesis of tuberculosis in young calves was that carried out by Dobberstein and Wilmes (1937), who administered to forty-one ten-day-old calves a single dose of a bovine culture (details of culture and dose not given). The calves were obtained from a herd free from tuberculosis and 20 of the 41 subsequently became infected. Half of the calves received the infective dose in a capsule and the remainder in milk from a flask fitted with a teat; 8 of the former and 12 of the latter became infected. The animals were killed at intervals varying from 22 to 149 days after receiving the dose. It is not possible to discuss the results in detail in this paper, but some of the most important are briefly mentioned. There were lesions in the mesenteric nodes in 12 calves (5 capsule, 7 contaminated milk), in 10 of which there were also intestinal tuberculous foci, always in Peyer's patches. These foci were very small (pin-head size) and found only on careful examination of the mucosa or by looking through the intestine from the serosal aspect. The supra-pharyngeal nodes were involved in 16 animals, the tonsils being affected in only 3 of these. Of the calves with throat lesions, 6 received the dose by capsule and it is suggested that rumination was responsible. It is doubtful, however, whether calves ruminate at ten days old, and it would seem to us more probable that the capsule lodged in the pharynx and the bacilli were liberated there. The liver showed no macroscopic lesions in any animal, but the portal node was positive microscopically in two animals and the liver in a third. The lungs showed tuberculosis in 3 calves (those allowed to survive the longest); the bronchial nodes were also involved. The latter alone showed lesions in a fourth calf. It is suggested that the lung lesions may have arisen secondarily from the lesions in the alimentary tract at an early stage in the infection when the calf still reacted by " primary complex " type of lesion; the view is expressed, however, that the lesions more probably resulted from return of the capsule to the mouth by rumination (regurgitation ?), followed by aspiration of some of the contents.

The earliest histological evidence of tuberculosis was seen twenty-two days after infection as productive lesions in a pharyngeal lymph node. Macroscopic evidence of caseation was first seen in the pharyngeal, mesenteric, and portal nodes in a calf killed twenty-nine days after infection. Microscopic evidence of calcification was observed first at fifty-one days and macroscopic evidence at eighty-eight days. Encapsulation and peripheral fibrosis respectively were seen after 136 and 149 days.

Somewhat similar experiments on a smaller scale are reported by Nieberle (1937), who administered varying doses of bovine tubercle culture to five three-weeks-old calves which had previously failed to react to the tuberculin test. The dose varied from 50·0 to 200·0 mg., given in milk and spread over 3 to 8 daily doses. In all five calves there were throat lesions when the animals were killed eleven to thirty-eight days after receiving the last dose. The lesions in the tonsils were in four cases seen only on histological examination, in the fifth calf (killed thirty-three days after the last dose) they could be seen with the unaided eye. In two of the calves the primary throat lesions were accompanied by primary tuberculosis of the small intestine and mesenteric nodes. One calf showed a tuberculous broncho-pneumonia of the aspiration type. No lesions of the portal lymph nodes are recorded (*cf.* our experiments with culture *direct* into duodenum; we also found no portal lesions when infected milk was given *per os*, but predominance of throat lesions). Of the remaining two calves one showed throat lesions only and the other had a few secondary lung lesions in addition.

A small experiment on similar lines has been described by Schumann and Fritzsche (1938), who used four calves three days old, obtained from first-calving cows which had failed to react to the tuberculin test. The calves were given milk from two cows with tuberculous mastitis. The first one received the milk (presumably from a bucket) from the third to the tenth days and was then given ordinary commercial milk (? pasteurised). It showed serious respiratory distress after a few days, lost condition rapidly, and was finally killed twenty-five days after the last infective feed. There was primary tuberculosis in the throat, lungs and intestines, together with generalisation. The second calf received a single dose of 2 litres of the contaminated milk by stomach tube and was killed in good condition thirty-one days later. The tuberculous lesions were confined to the small intestine (Peyer's patches) and mesenteric and gastric nodes. A third calf received contaminated milk from another cow with tuberculous mastitis for fourteen days and was killed in good condition fourteen days after the last dose. There was tuberculosis of the tonsils and suprapharyngeal nodes and lesions in the mesenteric nodes. A fourth calf was given by stomach tube a single dose of the same milk and killed 28 days later. There was no sign of tuberculosis. The second series of two calves received tuberculous milk which was lightly contaminated (tubercle bacilli demonstrable by guinea-pig inoculation only) as compared with the heavily contaminated milk used for the first two calves. No lesions in the portal lymph nodes are described in any of the calves.

A survey of 10,000 calves, varying in age up to three to four months, has been reported by Gofton (1937) in Scotland. There were 189 cases

(1·89 per cent.) of tuberculosis, of which 42 were considered to be congenital in origin. He states that the commonest lesions were found in the bronchial and mediastinal nodes, sometimes accompanied by lung lesions, and these constitute 60 per cent. of all cases of post-natal tuberculosis in young calves. He states: "Although I cannot prove it, I strongly suspect that quite a number of cases in which there are primary lesions confined to the bronchial or mediastinal nodes have their origin in alimentary infection." Edwards (1937) appears to have been led to the same conclusion. Neither author appears to have considered seriously the possibility—or probability—of primary lung infection by aspiration of infected milk in calves suckling infected cows or fed by ordinary or teat bucket with contaminated milk. It would seem more probable, in view of our own experiments and those of other workers here reviewed, that small infective doses which pass into the stomach are insufficient to produce intestinal or mesenteric node lesions, whereas aspiration of small numbers of bacilli into the lungs during feeding is sufficient to set up tuberculosis of the bronchial nodes, with or without macroscopic lung involvement. This is a more likely explanation than the view of Calmette—still expressed in the latest edition of his book (Calmette, 1936, p. 303)—that tubercle bacilli can pass through the intestine, remain "latent" in the mesenteric nodes, and then produce lung lesions without leaving any sign of their passage through the mesenteric nodes. Our experiments in which tubercle bacilli were introduced directly into the duodenum, thus effectively preventing all possibility of aspiration or regurgitation—a precaution not previously taken in experimental work—show that lesions always result in the mesenteric nodes with or without intestinal lesions and that a large dose is needed for infection; furthermore, that lung lesions rarely follow this route of infection, even after heavy doses. Another noteworthy point is that the portal lymph nodes are commonly involved, emphasising that lesions in these nodes are not necessarily indicative of liver infection since the nodes also drain the duodenum. Views on tuberculosis of the portal lymph nodes should be revised; isolated tuberculosis of these nodes in a young calf may indicate alimentary infection from the duodenum or congenital infection by the umbilical vein. The presence of a primary liver lesion would be necessary to prove the latter origin.

Schulz (1937) found 107 cases of tuberculosis among 10,000 calves 1 to 16 weeks old slaughtered at the Berlin abattoir. From a careful study of the pathological anatomy of the cases he concluded that in 54 animals the infection was aerogenous, in 42 it was congenital, and in only 7 was there evidence of primary intestinal infection. In the remaining 4 calves it was not possible to decide on the portal of entry of the tubercle

bacilli. Evidence of primary aerogenous infection, as shown by tuberculosis confined to the lungs, bronchial nodes, or both, was found in calves as young as 3 weeks. The earliest evidence of primary alimentary infection in the form of tuberculosis of the small intestine and mesenteric nodes was found at 4 weeks. Of special interest was the finding of tuberculosis of the bronchial nodes with calcification in calves only 3 weeks old; this pointed to intra-uterine infection which may have resulted from aspiration of infected amniotic fluid *in utero*.

The pathological findings in the unfortunate accident a few years ago at Lübeck (Schürmann and Kleinschmidt, 1935) throw considerable light on the pathogenesis of tuberculosis in young children, and this is of interest in relation to experiments on calves. A virulent culture of tubercle bacilli was accidentally administered to 251 very young children, of whom 72 died of tuberculosis. Autopsies were carried out on 68 of them and the lesions are described in detail, with special reference to their pathogenesis. All doses of culture—supposed to have been B.C.G.—were given *per os* and in some cases the child's nose was compressed and some of the children vomited. There were lesions in the mesenteric nodes in 60 cases and in all except one there was also intestinal tuberculosis. There were 5 cases of primary lung tuberculosis, considered to be due to aspiration. The findings constitute an effective contradiction of Calmette's views, for, if the latter's suggestions are correct, lung lesions should have been extremely common and mesenteric node lesions very rare, whereas in fact the reverse was found. The findings are those of a large-scale feeding experiment and do not agree with those observed on autopsies in children naturally infected with tuberculosis; in these there is a predominance of primary respiratory lesions indicating inhalation and not ingestion as the main source of infection. Caseation was observed in the cervical nodes of a child dying from generalised tuberculosis forty-four days after receiving the infected material; calcification was first seen at fifty-eight days. Other lesions recorded included 52 cases with affection of the deep cervical nodes, 42 of which showed tonsillar lesions, and 8 cases of tuberculosis of the middle ear, of which 6 were primary.

## Own Results

*Calcification.*—The earliest microscopic evidence of calcification, as shown by a basophil deposit in the centre of caseous areas, was seen at twenty-four days (calf 22, given 1·0 mg. into the trachea). Similar appearances were seen at thirty-six and forty-one days in two other calves. The first macroscopic evidence of calcification was observed at fifty-four days (calf 18, 80·0 mg. into duodenum); it was also seen at fifty-eight days.

*Tuberculosis of Hepatic or Portal Node.*—All calves receiving a dose of tubercle bacilli directly into the duodenum and surviving the operation showed tuberculosis of this lymph node either macroscopically or in histological section. When the dose was given by the ordinary or teat bucket there were no lesions in this node. In the case of calf 22 which received an intratracheal injection, the portal node was positive on guinea-pig inoculation; this was probably due to coughing and subsequent swallowing of bacilli. Excluding this case, tuberculosis of the portal node was always accompanied by involvement of the mesenteric nodes.

*Spread from Primary Sites.*—The lesions remained localised to one or more primary sites in all animals except calf 14 in which there was secondary miliary tuberculosis of the lungs and tubercles in the spleen. No liver or kidney lesions were encountered.

It appears that the mediastinal nodes are very rapidly infected, either from the mesenteric or portal nodes or from the pharyngeal, cervical, or bronchial nodes. Thus, in calf 12 there were tubercle bacilli present in the mediastinal node seventeen days after the administration into the duodenum of 1·0 mg. of culture. Two other calves showed infection of the mediastinal nodes after twenty-three days—calf 17 after receiving 80·0 mg. into the duodenum and calf 19 after receiving 1·0 mg. by teat bucket. In calf 22 the anterior mediastinal node showed histological evidence of tuberculosis twenty-four days after the intra-tracheal injection of 1·0 mg. of culture. Macroscopic caseation was seen as early as twenty-seven days—calf 6 infected with tuberculous mastitis milk. Calcification was seen at this site in only two calves, numbers 2 and 4, which received slightly contaminated milk by bucket and tube (regurgitated) fifty-nine days previously. In general, it seemed that the anterior mediastinal node was more rapidly involved, the portal of entry being throat, lungs, or trachea. The posterior mediastinal node was involved after a slightly longer interval following intestinal infection.

## General Conclusions

When young calves are given contaminated milk by ordinary or teat bucket it would appear that the throat and lungs are most readily infected; the intestines and mesenteric nodes are involved only with large doses or not at all, due in part to the bactericidal effect of the stomach contents. Primary infection of the lungs in such calves is due to aspiration, and this cannot be prevented by the use of a stomach tube because of the risk of regurgitation or rumination. The only effective method of limiting the portal of entry to the intestine is the introduction of the bacilli directly into its lumen. Much of the earlier work is of little value because of the

failure to observe these precautions, and this has led some to assume the passage through the intestine of tubercle bacilli without leaving visible lesions until they reached the lung; in such experiments the lung lesions have almost certainly been primary, and due to inhalation or aspiration of contaminated material given by the mouth from a bucket or flask or even by stomach tube. The frequency of throat lesions in calves experimentally given tubercle bacilli by these routes, as well as in children in the Lübeck disaster, affords conclusive evidence of the route of infection.

The probable explanation of the results obtained by Edwards (1937) is that aspiration of the slightly contaminated milk produced primary lung lesions in many of the calves, the dose being insufficient to cause intestinal or mesenteric node lesions. The absence of throat lesions is, however, remarkable. It is possible that histological examination or guinea-pig inoculation might have revealed lesions at this site. Edwards's conclusion that alimentary infection is of great importance in calf tuberculosis and results in lesions localised to the thoracic cavity is not, in our opinion, correct. The explanation is that teat or ordinary bucket feeding in young calves, with their well-known propensity for immersing their head in the bucket and splashing the milk throughout the naso-pharynx, affords an excellent opportunity for primary throat or aspiration tuberculosis.

The great difficulty of producing lung lesions by the intratracheal inoculation of cultures of tubercle bacilli was confirmed by us. The intratracheal injection of 1·0 mg. produced only a local lesion with involvement of the regional cervical nodes, and the presence of tubercle bacilli without visible lesions in the bronchial and mediastinal nodes revealed by guinea-pig inoculation. It is probable that this method of administration fails to transfer the bacilli into the alveoli of the lung; they are collected in the mucous secretions of the bronchi and destroyed or transferred to the pharynx, where some may be swallowed. In contrast to this, inhalation of very small doses of tubercle bacilli in the air very readily produces lung lesions. Furthermore, the use of a spray through a tracheotomy wound is also effective in producing primary lung lesions; *e.g.*, Findel, quoted by M'Fadyean (1910), gave 3·0 mg. of culture to a calf in this way and the animal had to be killed *in extremis* twenty-five days later, when it showed tuberculosis of the lungs and bronchial and mediastinal nodes, the abdominal nodes being unaffected. By the use of a spray, passage of contaminated material direct into the alveoli is facilitated, and this probably fails to occur when fluid is injected into the trachea.

**Summary**

The pathogenesis of tuberculosis in young calves was studied in a series of twenty-four animals from a tuberculosis-free herd, given, when seven days old, an infective dose in the form of either naturally contaminated milk (ordinary raw bulk milk or undiluted milk from cows with tuberculous mastitis) or a virulent culture of bovine tubercle bacilli.

The infective dose was given by various routes: ordinary and teat bucket, stomach tube, directly into the duodenum, and intra-tracheally. The pathogenesis was studied at autopsy, supplemented by histological examination and guinea-pig inoculation.

The results are discussed with especial reference to the pathogenesis of tuberculosis in young calves naturally infected by contaminated milk either by suckling or by bucket feeding.

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# BESNIER-BOECK'S DISEASE

## A REVIEW

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### Introduction

BESNIER-BOECK'S disease is a systematised disease of lympho-reticular (reticulo-endothelial) tissue, presenting clinical features of a chronic infectious granuloma. It persists often for years, sometimes spreading slowly from one organ or tissue of the body to another, frequently relapsing, resistant to treatment but at times healing spontaneously, and characterised by only slight constitutional reactions.

The clinical manifestations are characteristic cutaneous lesions; enlargement of the superficial lymph nodes, tonsils, parotid and lachrymal glands; widening of the hilar shadows and infiltration of the peripheral fields of the lungs as observed roentgenographically; rhinitis, iridocyclitis, splenomegaly and hepatomegaly. The pituitary gland and the skeleton are sometimes involved. These clinical manifestations have been recognised, within comparatively recent years, as different expressions of a single pathological process, the ætiology of which still remains undetermined.

The terminology of sarcoidosis is confusing and involved. The more common terms used are: Boeck's, Besnier's, Hutchinson's, Mortimer's, or Schaumann's disease (or any combination of the foregoing names); "lupus pernio" (Besnier); "sarcoid" (Boeck); "benignes miliar lupoid" (Boeck); "benign lymphogranulomatosis" (Schaumann); "ostitis tuberculosa multiplex cystoides" (Jungling); "multiple benign sarcoid" and "multiple benign lupoid." In May of 1934 the Réunion Dermatologique de Strasbourg devoted itself entirely to the consideration of "sarcoid." At this meeting Kissmeyer agreed to the suggestion that the name he had bestowed upon the condition be changed from "la maladie de Boeck" to "la maladie Besnier-Boeck."

### Historical Note

Hunter (1936) has published an excellent historical account of the early contributions to the subject. He records that the disease was first described by Jonathan Hutchinson, who observed a patient in 1869 with peculiar purplish, raised lesions on the front of the legs, on the fingers and on one forearm. These lesions were irregular in size and shape, possessed sharp margins and smooth surfaces and were neither tender nor painful. In his

*Illustrations of Clinical Surgery* Hutchinson (1875) described the disease in detail, and after a year's observation remarked that medicines of various sorts had not affected the lesions.

Besnier (1889) gave a more elaborate account of a patient with large violaceous swellings of the nose, ears, and over the interphalangeal joints of the fingers. He remarked upon the absence of ulceration, the enlargement of cubital lymph nodes and upon the longitudinal striation of the fingernails. He considered the condition different from that described by Hutchinson and called it " lupus pernio " (chilblain lupus).

There are subsequent records of cases published by Tenneson (1892), and again by Hutchinson (1898), who called the condition " Mortimer's malady," after the name of his patient.

Boeck (1899) described for the first time the clinical picture and microscopical structure of a characteristic skin affection to which he gave the name of " multiple benign sarcoid of the skin " because he believed that it resembled the small cells of sarcoma. In later publications Boeck (1905, 1916) recorded his clinical and histological examinations of several more cases and noted that the disease may affect lymph nodes, mucous membranes, bones and internal organs. He finally considered it an infectious process nearly related to tuberculosis and possibly due to the tubercle bacillus. He re-named the condition " benignes miliar lupoid."

The next important contributions came from roentgenologists. Kienbock (1902) noted on X-ray examination curious " cysts " in the digits and toes of a twenty-seven-year-old patient who had acquired syphilis five years previously. He was ignorant of their relation to sarcoid and attributed the findings to lues. Kreibech (1904) associated similar lesions with " lupus pernio." Remijnse (1907) reported a patient with " dactylitis syphilitica " accompanied by generalised lymphadenopathy; there was no definite evidence of congenital or acquired lues, nor any lesions in the skin: the skiagrams of the osseous changes would now be considered characteristic of sarcoid. Rieder (1910) described the X-ray appearance of the phalanges in two of his patients and observed that both of them had active " lupus pernio."

Benzacon and Labbe (1911) briefly described and pictured accurately what they considered to be a particular form of tuberculous adenitis which seems to correspond closely to the changes now recognised as characteristic of sarcoid.

Involvement of the internal organs was first noted by Kuznitzky and Bittorf (1915). A biopsy of the skin lesion showed the morbid histology pictured by Boeck. Their patient presented miliary lesions in the skin, enlargement of the lymph nodes, spleen and liver. Involvement of the hilar glands and mottled infiltration of the peripheral fields of the lungs

were also demonstrated radiologically. This is the first case reported in which the lungs were shown to be definitely affected. These writers did not regard the disease as tuberculous but as a generalised disease of unknown ætiology.

Schaumann (1917, 1923, 1924, 1926, 1936) confirmed and enlarged the conceptions of Boeck. He demonstrated that Boeck's sarcoid and lupus pernio are histologically one and the same disease.

Jungling (1919) described the " cystic " changes in the bones seen on X-ray examination, and he concluded from histological examination of the soft tissues of the finger that the process was a peculiar form of tuberculosis. He gave to the bony deformations the term " ostitis tuberculosa multiplex cystica." He later (1928) recognised the close association between this disease of the bones and both Boeck's sarcoid and lupus pernio Jungling pointed out the fact that the periosteum and joints were spared in a process that caused extensive alteration in the medullary portions of the phalanges. He referred to the histological changes as tuberculoid reactions and was further confirmed in his opinion that the disease was a peculiar form of tuberculosis.

The most important contribution of recent years is probably Kissmeyer's (1932). He summarised the previous contributions to our knowledge of the disease and included many original observations of his own. Other important papers are those of Rischin (1922); Martenstein (1924); Bernstein (1927); Goeckerman (1928); Bernstein, Konzlemann and Sidlick (1929); Doub and Menagh (1929); Kirklin and Morton (1931); Funk (1933); Bayer (1933); Bergel and Scharff (1933); Sannicandro (1934); Pautier (1935). In all these papers there are reports of cases, descriptions of the pathological lesions, clinical discussions, and many controversial statements concerning the ætiology of the disease.

The name " sarcoid " was derived from two Greek roots meaning " flesh " and " form." Boeck gave this name to the condition he described because he believed that the histological picture resembled the small cells of sarcoma. But the disease has in reality nothing in common with true sarcoma, resembling it neither in gross appearance, histology, nor in its clinical course.

## Ætiology

Many theories have been advanced in attempting to account for the cause of the disease. The appearance of the pathological lesions has led almost inevitably to the belief that the disease is tuberculous, but this contention has never been proved and has resulted in endless controversy on the subject. Proof that the disease is tuberculous demands the finding

of tubercle bacilli in stained sections or following inoculation in animals. In the great majority of cases reported, however, these requirements have not been fulfilled. The negative results are usually interpreted as indicating that the tubercle bacillus is of the bovine strain and that the tissue allergy of the patient is high as a result of a previous tuberculous infection.

Boeck (1905) considered the disease a constitutional one with marked cutaneous symptoms caused by a non-virulent variety of the tubercle bacillus. Schaumann (1917) also was of the opinion that the cause of sarcoidosis is a benign form of tubercle bacilli of the bovine type; whilst human tubercle bacilli may cause the formation of sarcoids if the infected person is an unsuitable soil for the tubercle bacillus. Bernstein (1938) states that about 10 per cent. of the reported cases have had coincident tuberculosis or subsequently developed tuberculosis of the lungs or other internal organs. There is a growing tendency to consider tuberculosis as the ætiological agent, an opinion held by Bloch (1907, 1916), Volk (1913), Martenstein (1921), Goeckerman (1928), Jadassohn (1934) and Montgomery (1937).

Kyrle (1921, 1927) has demonstrated tubercle bacilli in an early sarcoid lesion in two instances. He believed that sarcoidosis was a foreign body type of response to the products of disintegration of the tubercle bacillus. Wende (1911) also claimed to have found tubercle bacilli in early lesions. Continued efforts along this line have failed to confirm these findings.

Goeckerman (1928) stressed the finding of tubercle bacilli in the early lesions, and believed that a greater number of positive results would be obtained in stained sections and following inoculation in animals if early lesions were removed instead of the older classic ones. Pautrier and Glasser (1936) reported a case of sarcoid of the skin, and claimed to have produced a lesion at the site of an experimental inoculation in one of two rabbits and to have demonstrated acid-fast bacilli, presumably of the bovine type, in the lesion. They stated that the original skin lesion had a " structure more tuberculous than usual."

The evidence in favour of the tubercle bacillus as an ætiological agent in uveo-parotid fever is ably presented by Garland and Thomson (1933). The fact that some cases are complicated by tuberculosis does not prove the tuberculous nature of the disease. Pautrier (1937) states that tuberculosis develops in such cases on a ground already weakened by another infection. Moreover it is known that the disease occurs frequently in northern countries where tuberculosis is especially rare.

Another hypothesis is that the condition is a non-specific tissue response which may be evoked by a variety of pathogenic agents such as the tubercle bacillus, the leprosy bacillus, the *Spirochæta pallida* and *leishmania*. This

view is frequently put forward in dermatological writings. Darier (1934) believed that sarcoidosis is a uniform reaction of the body against a multiplicity of possible stimuli of which the tubercle bacillus, possibly in its filterable form, is one. Sulzberger (1936) states: "A sarcoid reaction must be considered simply as a characteristic histologic response in a certain type of immunologic tissue reaction. It so happens that this type of reaction is in most cases caused by the tubercle bacillus."

Experimental studies have shown that the epithelioid cell response—*i.e.*, the sarcoid response—may be caused by the presence of lipoids in the bacillus of tuberculosis. Ray and Shipman (1923) found a similar substance in grass and in colon bacilli and produced a sarcoid reaction with it. Sabin (1932) produced the sarcoid reaction with the lipoid fraction of phosphatide, while Krause (1927) pointed out that sarcoid formation is the first response to an animal free from tuberculosis (pre-existing or active), to living or dead tubercle bacilli, and is later altered when allergy to the tuberculous pyrines develops. Hence it would seem that sarcoid formation is not a specific response to the tubercle bacillus.

Another hypothesis is that Besnier-Boeck's disease is a systematised disease of lympho-reticular (reticulo-endothelial) tissue comparable to Hodgkin's disease and leucosis, and should rank as a reticulosis (Pullinger, 1932; Ross, 1933; Bodley Scott and Robb Smith, 1936; Bodley Scott, 1938).

Kuznitsky and Bittorf (1915) were the first to suggest that sarcoid represents a disease *sui generis*. Rischin (1922) and Whittemore (1925) came to the same conclusion, and the latter reported a case in which he established that sepsis was the cause.

Syphilis as a cause of the disease has been stressed by Frazier and Hu (1933) and by Pautrier (1914). These authors reported cases of cutaneous sarcoid in patients with a positive Wassermann reaction, with disappearance of the lesions under anti-syphilitic treatment. The majority of the reported cases, however, have a negative serologic reaction.

Finally, Kissmeyer and Nielsen (1934) believe that Boeck's sarcoid is a chronic infectious granuloma, and they postulate that it might be a virus infection and that it is a separate pathologic entity. Led by analogy to lymphogranuloma inguinale, Williams and Nickerson (1935) prepared an antigen from the sarcoid tissue which in four cases produced skin reactions within twenty-four hours, by intradermal test.

The diagnosis of sarcoid was proved in two cases by resections of the intestine, which microscopically showed the characteristic sarcoid lesion. These authors suggest that, like lymphogranuloma inguinale, sarcoidosis is probably a virus disease. If this work is substantiated on a larger series of

cases it would seem a more rational explanation than that the disease is an atypical form of tuberculosis. The use of this antigen may also enable a positive diagnosis to be made before the appearance of skin lesions, and cases with prolonged fever of unknown origin may be diagnosed by a skin test.

Pautrier (1936) believes the condition to be an autonomous infectious granulomatosis due to a new virus which may be placed between those of tuberculosis and leprosy.

### Incidence

The incidence of sarcoidosis is not known. Bodley Scott (1938) reported that in over 300 histological examinations of lymph nodes excised to establish a diagnosis of Hodgkin's disease, sarcoidosis was found once in every eleven cases. This author collected eight cases at St. Bartholomew's Hospital, London, in less than a year.

In Kissmeyer's (1923) series of 200 patients, at least half the cases contracted the disease before the age of thirty. The sexes were affected almost equally. The disease occurs in both white and coloured races. A fair proportion of cases have been reported from the Scandinavian countries, where the disease seems to be comparatively common. Many of those reported from the United States have been in patients of the coloured race.

Pinner (1938) found in the literature seventeen necropsy reports on patients with sarcoid lesions and he added another of his own.

### Pathology

*Autopsies.*—Pinner (1938) has analysed the findings at the 18 necropsies reported in the literature. Out of these 18 cases, 10 died of causes either not related to sarcoid or of causes not fully stated; in the remaining 8, sarcoid or its consequences was the direct cause of death. In 2 of these the location of the lesion (in one in the region of the optic chiasm, and in the other in the pituitary gland) was responsible for the fatal issue. In only one (Nickerson, 1937) was it believed that the massiveness of the general involvement *per se* caused death. One patient died with emphysema as the principal lesion, and here the massive and diffuse hyalinisation of the intrapulmonary granulomata was the direct cause of the fibrosis and concomitant emphysema. This case lends a solid anatomical basis to the X-ray interpretation of fibrosis developing following sarcoid lesions in the lung. In 4 of the 18 cases, pulmonary tuberculosis was the cause of death; in a few other cases less significant tuberculous foci were found in addition.

Pinner confirms Schaumann's (1934) impression that frank caseating

tuberculosis in this disease seems to be a direct transformation of the sarcoid lesions and not an added, separate process. This impression was gained by the fact that small caseous centres were found in foci that otherwise presented typical sarcoid structure. Single foci may accordingly present typical tuberculous structure. In two of Schaumann's cases the cutaneous lesions of sarcoid (lupus pernio) disappeared simultaneously with the development of bacilliferous tuberculosis; and in two others he made the identical clinical observation of disappearing cutaneous sarcoids at the time of the appearance of tuberculosis and the development of hitherto absent tuberculin allergy.

In practically all the necropsies more lesions were found than were clinically diagnosed. It was striking that the most frequent site of sarcoid involvement followed closely the pattern of distribution in miliary tuberculosis; lymph nodes, lung, liver, spleen and bone marrow being the tissues most frequently affected.

*Histology.*—Wherever the sarcoid lesion is found, whether in the skin, lymph glands or internal organs—allowing for differences in the texture of the tissues themselves—the histological features are essentially the same.

These lesions appear as collections of large epithelioid cells arranged in the form of miliary tubercles, sometimes lying as isolated structures in a comparatively normal tissue and sometimes in groups or strands. These collections of cells may attain such large proportions that they replace most of the normal tissue. They are not as a rule outlined by an inflammatory zone of lymphoid cells, and a characteristic feature is the absence of inflammatory reaction in the surrounding tissue. Occasionally one or more large giant cell of the type of the Langhans cell occurs at the centre or more rarely at the periphery of the " tubercle." There is an absence of necrosis giving rise to caseous matter and calcification. The lesion resembles an epithelioid (miliary) tubercle. There is a marked tendency to fibrous degeneration. The lesion retains this appearance in sections of the skin or lymph nodes that have been affected for months or years. Healing may, however, occur through fibrosis.

Beitema (1934) has described and illustrated the miliary nodules in the lung. Here, too, the miliary lupoid lies isolated in the alveolar wall without a surrounding inflammatory zone.

The histological picture described above does not encompass the entire life cycle of the lesion. It does not include the earliest nor the late phases, for, according to clinical and radiological observations, these must include resorption and fibrosis.

Longcope (1936) states : " The histological picture is similar to the picture of the pathological condition which Dr. Sabin gets in rabbits and guinea-pigs

by the injection of the phosphatide fraction of the tubercle bacillus and a pure crystalline acid obtained from this phosphatide prepared by Dr. Anderson of Yale and known as phthioic acid."

*Bacteriology.*—A large number of attempts have been made to demonstrate tubercle bacilli in the specific lesions. Kissmeyer (1932) stated that he had found in the literature 39 cases of Boeck's sarcoid in which animal inoculation was done and that 7 of them had given what seemed to be positive results. In 4 of these 7 cases he considered that the usual form of tuberculosis was also present. Jungling (1928) reports one positive result with inoculations of a subcutaneous node, the guinea-pig dying of tuberculosis in seven months. Pautrier (1937) reports one positive inoculation from the lymph node of a patient giving a positive tuberculin reaction.

Pinner (1938) has summarised all positive bacteriological findings in the literature. Their number is very small, and the number of completely convincing positive results is insignificant. Practically all positive animal inoculations are represented by extremely slowly progressive disease or by atypical findings, such as strictly localised lesions, or tuberculous manifestations occurring only after animal passage. For this reason the reliability of these findings is questioned and the likelihood of spontaneous infection is suggested. All these arguments are inconclusive, since the original authors often omit the description that could identify an inoculation tuberculosis.

On the other hand, Schaumann (1934) and Ramel (1934) state that though tuberculosis was not produced by inoculating material from cases of sarcoid in the first generation of guinea-pigs, the further inoculations of lymph nodes from the first generation of guinea-pigs through two or three generations resulted in some instances in the production of tuberculosis. It has been suggested that in such instances the disease was caused by a " filterable " form of tubercle bacilli.

Acid-fast bacilli have been demonstrated only rarely in tissue sections. Kyrle (1921) examined repeated biopsies from a patient with acute exacerbations of cutaneous sarcoid. During the early inflammatory phase many acid-fast bacilli were seen ten days after the onset; eleven days later only a few acid-fast bacilli were seen while the typical sarcoid structures had made their appearance; in later biopsies no acid-fast bacilli were seen. These observations probably explain both the positive and negative findings of different workers. During one of the febrile prodromal phases Kyrle injected 5 c.c. of blood into a guinea-pig and into another one simultaneously skin material; the first guinea-pig developed tuberculosis, the second did not. Kyrle concluded from this experiment that the bacilli are killed promptly

in the skin. It seems probable that tubercle bacilli may be present in sarcoid lesions only during the earliest phases of their development.

*Tuberculin Reaction.*—The great majority of patients have a lasting hypo-sensitivity or anergy to tuberculin (lack of reaction to high concentrations of tuberculin).

Kissmeyer (1932) found that a positive tuberculin reaction was noted in about 40 per cent. of those reported, and that when it occurred it was usually a weak reaction. He concluded that the incidence of positive tuberculin reactions was approximately that which one would expect in any group of patients of the same age who did not have clinical tuberculosis. Kissmeyer also found that a focal tuberculin reaction was quite as unusual as a skin reaction. Of eighteen reported attempts to produce this reaction, fifteen were negative. Of nine attempts to produce this reaction in his own patients, all were negative.

Martenstein (1924) states that, of 82 patients with Boeck's sarcoid on whom tuberculin tests were done 73 per cent. gave a negative reaction, and 62 per cent. of 46 patients with " lupus pernio."

Funk (1933) and Schaumann (1924, 1934) have reported cases in which patients with sarcoidosis who gave a negative reaction showed later a positive tuberculin reaction after the development of proven pulmonary tuberculosis. Stein (1934) reports a similar finding after treatment with tuberculin.

Schaumann (1936) maintained that a negative Mantoux reaction changes to positive as the cutaneous lesions heal and disappear.

This anergy plays an important rôle in ætiological discussions. Those who uphold the view that the disease is caused by a reaction to tubercle bacilli explain the lack of skin sensitiveness upon Jadassohn's (1929) theory of cutaneous anergy. This specific anergy is regarded as due to the neutralisation of the tuberculo-pyrine of Eber-Sahli by the anticutin or procutin found in the serum and in the lesions by Martenstein and Nole (1929). In some patients with sarcoid lesions procutins and anticutins are demonstrable in the blood stream. In mixtures of serum and tuberculin, procutins enhance and anticutins neutralise the skin reacting factor in tuberculin.

Pinner (1939) studied the serum of three patients with sarcoidosis. The serum was mixed with equal amounts of OT, using undiluted serum, serum diluted 1 to 10 and in the third case 1 to 100. These tuberculin-serum mixtures and tuberculin-saline mixtures of equal strength were incubated at 37° C. for two hours; 0·1 c.c. of each mixture was injected intracutaneously in a known allergic person. The result was that all three sera depressed the skin reaction to a considerable degree. The true significance of this finding needs further study on a larger number of patients.

Lemming (1940) inoculated sarcoid patients with B.C.G., the effect of which is to produce tuberculin sensitiveness in a previously Mantoux-negative or " negatively anergic " normal individual. An inoculation of 0·05 mg. living B.C.G. given to a patient with typical uveo-parotitis had no effect; thrice the dose produced a local reaction and swelling of the regional lymph nodes, but a Mantoux test with 5 mg. of tuberculin was still negative. One of the affected nodes was excised and on examination it was found that the changes produced in it by B.C.G. were similar to those found in benign lymphogranulomatosis, rather than to those which are usually found after B.C.G. vaccination. The tissues had reacted to vaccination in the same way as they react in the disease itself. In another case in which mediastinal and other lymph nodes were involved repeated doses of B.C.G. failed to change the negative Mantoux reaction.

*Hæmatology.*—There may be at times slight anæmia in patients suffering from Besnier-Boeck's disease (Kissmeyer, 1932; Chevalier and Ely, 1934). These authors also point out that the total number of leucocytes is within normal limits, but a relative increase in the monocytes may occur. The monocytosis is the hæmatological manifestation of a monocytic proliferation leading to the epithelioid granuloma, and it only occurs during the actively proliferating phase. An eosinophilia has been noted by Longcope and Pierson (1937).

Salvesen also noted a frequent increase of the rod-shaped polynuclears with a shift to the left.

Polycythæmia due to the secondary pulmonary fibrosis may also occur. An increase in the erythrocyte sedimentation rate is reported by Snapper (1938).

Salvesen (1935) has observed a very striking increase in the total serum proteins in three out of four patients with generalised sarcoidosis. The total serum proteins varied from 9·0 to 9·69 grams per cent. The unusual figure was due principally to an increase in the globulin fraction, with a range from 5·05 to 6·10 per cent. The plasma albumin remained normal. In these changes the disease resembles multiple myelomatosis, lymphogranuloma inguinale and kala-azar.

### Clinical Features

Besnier-Boeck's disease usually starts in early adult life. The onset is insidious and the disease produces obvious changes, most often in the skin, in the lymph nodes, in the bones of the hands and feet, or in the lungs. In a few instances the earliest pronounced symptoms have been referable to an involvement of the lungs. The course of the disease is extremely chronic.

In the majority of cases such symptoms of intoxication as pyrexia or emaciation are absent, although there may be complaint of tiredness.

The disease may present a number of different syndromes because the dissemination of sarcoids may take place in many organs of the body. On the basis of clinical observation, supported by biopsy findings, there is hardly any organ that may not be involved. Boeck originally pointed out that sarcoids often develop in the skin, and there are many patients who show only the cutaneous eruption. Others show the skin lesions and visceral lesions as well, and there are others again in whom the visceral organs are the only ones to be affected. In many instances the cutaneous eruption is merely a visible indication of a systemic disease, and it is important to realise that sarcoidosis is potentially a generalised granuloma in which the skin manifestations are frequent but not constant. There have been many instances where systemic complaints antedate the onset of the dermatosis, and it is probable that as the systemic nature of the disease becomes more generally known, systemic lesions will be found in an even greater proportion of cases. The frequency of the cutaneous lesions is difficult to compute, but it is probable that they are found in not more than half of all the cases.

*Cutaneous Lesions.*—The majority of the cases have been reported as examples of an eruption of the skin, affecting usually the face, the ears, the nose and the extremities.

The following is Hutchinson's (1875) description of the lesions in his original case:

" On the front of his legs, some of his fingers and on one forearm were a number of patches consisting in the first instance of distinct tubercles, which afterwards became confluent and then lost their tuberculous character. The patches were peculiar chiefly on account of their dark purple colour; this tint seemed to depend partly upon venous congestion and partly upon deposit of colouring matter in the tissues, for although their margins could be made pale by pressure, no amount of squeezing altered the colour of the central parts. The patches were irregular in size and shape, distinctly raised above the general surface, their margins for the most part irregular and abruptly defined, and their surface smooth and almost glossy, or sometimes covered with thin, dry epidermic scales. Their elevation above the surrounding skin was due in great part to œdema, for they could be made to pit by continued pressure and in fact could be squeezed until all thickening disappeared. They were neither tender nor painful. The skin around them was slightly œdematous."

It is evident that this patient suffered from lupus pernio. Clinically the cutaneous lesions fall into four groups:

1. *Lupus pernio* (Besnier, 1889; Tenneson, 1892).—The lesions of lupus pernio often develop on the tip of the nose, on the cheeks, on the lobes of the ears, on the fingers and toes, as red or blue-violet, often brownish, infiltrations of the skin, localised in the subcutaneous tissue. The eruption may have a sharp border.

The reddish-blue colour is due to the formation of telangiectases. They bear a certain resemblance to the lesions of chilblains. There is frequently scaling of the skin, but ulceration never develops. If the lesion disappears a brownish scar remains. Associated bone changes are common when the fingers are affected.

2. *Miliary lupoid* (Boeck, 1899, 1905).—There are two forms described; the first is a fine eruption of small red papules affecting the cheeks, forehead, extensor surfaces of the arms, the buttocks and the back of the legs. The papules are usually smooth but may show hyperkeratosis. This form may occur in plaques resembling lichen planus (lichenoid variety). The second form is the nodular variety, which may develop in any part of the skin either as small red or bluish or brown nodules or as larger diffuse infiltrations. They are usually very persistent, they sometimes itch and scale but never ulcerate. In the stage of involution central flattening may give rise to an annular appearance and telangiectasis and pigmentation of the margins are common. Under diascopic pressure these nodules are composed of greyish-yellow tissue which first suggested the name of " miliary lupoid."

3. *Angio-lupoid* (Brocq and Pautrier, 1913).—This form is less common and consists of soft infiltrated plaques on the sides of the root of the nose. They are violet-red in colour and are markedly telangiectatic.

4. *Erythrodermie sarcoïdique* (Schaumann, 1924).—This rare form appears as large superficial serpiginous red areas on the front of the legs and thighs.

*Lymphadenopathy and Splenomegaly.*—In Boeck's first case the cutaneous sarcoids were complicated by general swelling of the lymph glands. The lymph nodes are very frequently enlarged, sometimes to a considerable degree. Both the regional and distant lymph nodes may be involved in the process. The sarcoids may spread through the lymph glands of the body and so result in a generalised lymphadenopathy. This enlargement may be generalised, or it may be more pronounced in some regions or localised to groups of nodes such as the inguinal and femoral, the epitrochlear and axillary, or the submental and submaxillary. There is no regional relationship to the lesions of the skin.

Schaumann (1936) states that he has found lymphatic involvement in all his clinical cases, and that in 21 of his active cases in which the tonsils were examined they were found to be involved. The mucosæ of the mouth, nose, naso-pharynx and larynx are also affected sometimes.

A site commonly affected is the glands of the hilum of the lungs. This is only revealed by the skiagram usually and may give rise to a radiological picture similar to that of tuberculous glands. If they are of considerable size a diagnosis of tumour may be suggested.

Martenstein (1924) states that of 34 cases with chest radiograms 31 per cent. showed enlargement of hilar lymph nodes. The intra-abdominal lymph nodes are most probably involved in the majority of cases but their detection is extremely difficult.

The enlarged nodes are smooth, painless and insensitive, discreet and freely mobile. The lymphatic lesions usually evolve unnoticed and must be searched for systematically.

Splenomegaly is common in this disease. The enlargement of the spleen may be considerable and the organ has a firm consistency with a round edge. Some cases reported as tuberculous splenomegaly with miliary tuberculosis of the lungs may quite possibly be instances of sarcoidosis (Hickling, 1938).

*Pulmonary Lesions.*—The periadventitial cells of the smaller arteries in the interalveolar septa are active elements of the reticulo-endothelial system. The sarcoids are frequently localised in the lungs. Kissmeyer (1932) emphasises the frequency with which the bronchial lymph nodes and the lungs are involved. Skiagrams of the chest disclosed enlarged peribronchial lymph nodes in 19 of 24 cases, and in 15 of the 24 there were increased hilar shadows. In 5 cases the lungs showed the marbled or reticulated appearance referred to by many authors. This produces an effect that may resemble miliary tuberculosis, and in some instances they resemble the shadows observed in some cases of pneumoconiosis. A characteristic of these shadows is that they extend from the roots of the lung towards the bases and not usually in the direction of the upper lobes or apices.

There is as a rule little or no elevation of temperature. Cough and expectoration may occur. When the superior mediastinal and peribronchial lymph nodes are greatly enlarged dullness over the manubrium and in the interscapular spaces may be elicited and the breath sounds may be broncho-vesicular in character. Râles are rarely heard.

The miliary lesion may result in the volume of the blood stream passing through the lungs becoming reduced and the right ventricle has to overcome the increased resistance. These cases may develop dyspnœa and cyanosis with right ventricular enlargement followed by progressive myocardial failure.

The pulmonary lesions may be pronounced, may evolve without symptoms, and are not usually demonstrable clinically. Radiographic examination is always necessary and very often the involvement is revealed as a complete surprise.

Four distinct radiological appearances may be encountered.

1. Enlargement of mediastinal or hilar lymph nodes. These are usually bilateral and give large dense shadows with radiations extending into the lung fields, most often directed along the medial portion of the lower lobes towards the bases. These shadows may simulate those of Hodgkin's disease or new growth.

2. Enlargement of the hilar glands may lead to compression of a bronchus, giving rise to atelectasis.

3. A chronic interstitial fibrosis may be seen which is similar to that seen in chronic fibrotic tuberculosis. This is caused by the tendency of the sarcoids to undergo fibrotic degeneration, becoming completely replaced in time by connective tissue.

4. There may be a multitude of miliary foci more or less evenly and symmetrically distributed throughout both lungs and whose seeding is usually denser in the middle and lower portions of the lungs than in the apices. These nodules are dense and present fluffy contours. This diffuse mottling simulates that seen in cases of miliary tuberculosis, but it is usually coarser and less regularly disposed. These shadows are characterised by the absence of exudative features and by their stability.

The different forms of radiological appearance that may be seen are probably an expression of the different ages of the pulmonary lesions. The more fibrotic lesions are probably the older ones. The radiological shadows may gradually recede and disappear or they may remain unaltered for months or years as Michelsen (1931) observed. Nielsen (1934) mentions the possibility of resorption. Longcope and Pierson (1937) describe complete disappearance of hilar and parenchymal lesions in the course of six years in one of their cases, and in the course of ten years in another case.

Bodeker (1932) suggested that some cases reported as healed miliary tuberculosis of the lungs may be examples of pulmonary sarcoidosis.

*Skeleton.*—The reticulo-endothelium of the bone marrow is another site of predilection for the development of Boeck's sarcoids. The frequency of the bone lesions is difficult to judge. Nielsen (1934) in a special study of these lesions reported that approximately 20 per cent. of patients with Boeck's sarcoid examined at the Finsen Institute had demonstrable bone lesions.

Jungling (1919) described the remarkable changes in the bones. The characteristic affection nearly always develops in the phalanges of the fingers and toes, but in rare instances the long bones of the extremities are involved. When the fingers are affected with lupus pernio associated bone lesions are common. They are often accompanied by cyanosis, swelling and red-blue discoloration in the affected areas. This cyanotic swelling may resemble tuberculous dactylitis. There may be no external evidence

of disease, but usually the fingers are irregularly enlarged and the tips squared, with some dorsal flexion of the terminal phalanx. Subcutaneous nodules may appear about the interphalangeal joints. The fusiform swelling of the phalanges may be painful. In advanced cases malformations and mutilations of one or more fingers or toes may occur, and dystrophic changes of the nails may lead to gradual disappearance of the terminal phalanges.

The periosteum and joints are spared in a process that causes extensive alteration in the medullary portion of the phalanges. The normal structure of the phalanx is replaced by a lace-like network with small areas of rarefaction often surrounded by a zone of increased density. The apparent cystic condition consists, not of cystic changes but of granulomatous infiltration into the canals with destruction of portions of the medulla. It is the marrow that forms the starting-point of the alterations in the bones.

Syphilis, leprosy, tuberculosis, gonorrhœa and gout may cause changes in the bones closely resembling the lesions described. Jungling called the condition " ostitis tuberculosa multiplex cystica," but this term should be abandoned now that we know that the bone lesions are but one of the manifestations of sarcoidosis. The course pursued by these bony lesions is very chronic. After many years the bone and cutaneous symptoms may disappear spontaneously, but the X-ray may still show minute cysts which are the remnants of the condition.

Radiologically three different types of bone lesions are recognised.

1. Multiple, circular, punched-out areas of rarefaction and reticulation distributed through the medulla of the phalanges, metacarpals or metatarsals, with irregular enlargement and distortion of the bones, but not involving the periosteum or joints.

2. The bone structure may be modified by a generalised dissemination of sarcoids. Multiple minute areas of bone resorption give rise to a lattice-like appearance of the phalanges.

3. There may be a general atrophy of the skeleton of the hands and feet. This is caused by a generalised dissemination in the reticulum of the bone marrow in which the sarcoids are confluent and individual lesions are too small to be distinguished.

*Eye Lesions.*—The eyes are commonly affected. Here the dissemination of nodules in the iris and corpus ciliare explains the frequency with which symptoms of iridocyclitis are found. Blegvard (1931) states that iridocyclitis occurs in about 10 per cent. of cases of sarcoidosis. It is usually first seen by the ophthalmologists and diagnosed as tuberculous or paratuberculous iridocyclitis.

A problem of interest is the possible tuberculous nature of chronic

iridocyclitis. That a tuberculous iridocyclitis exists, and that iridocyclitis is seen in many syndromes now suspected to be of tuberculous origin, make it possible that the usual type of slowly progressive iridocyclitis may be yet another abortive manifestation of tuberculosis. Brooks, Juler and Williams (1940) have reported a series of forty cases of chronic iridocyclitis in which they found radiological and clinical evidence suggestive of tuberculosis in no fewer than twenty-five patients. Frank tuberculosis as shown by bacilli in the sputum was present in only three patients, but the incidence of suggestive lesions in the chest and elsewhere is certainly far higher than a statistical computation for the general population would show. A point of interest that they bring out is the relative insensitivity of the Mantoux test in cases in which the evidence for tuberculosis was definite. This agrees with the findings of other observers, and emphasises the fact that skin sensitivity to tuberculin is not such a conclusive criterion of the nature of localised lesions as was once believed.

This affection is very resistant to treatment and may lead to blindness. Mylius (1928) has recorded an instance of bilateral iridocyclitis and Ernsting (1937) has reported a case in which the eyelid was involved. Blegvard (1931) has recorded others with conjunctival affection.

*Other Lesions.*—Swelling of the parotid glands due to the presence of sarcoids has often been noted. If iridocyclitis is present at the same time these patients then present a syndrome resembling uveo-parotid fever. This clinical syndrome was first clearly described and differentiated from mumps by Heerfordt in 1909. It is a fairly rare condition, but it is now recognised as part of the syndrome of sarcoidosis. It is regarded by many competent authorities as an abortive form of tuberculosis, ending sometimes in a frank generalised outbreak of the disease. The histological character is that of tuberculosis without caseation and is identical with that found in sarcoidosis. Slot, Goedbloed and Goslings (1938) and Pautrier (1938) have reported instances which show clearly that uveo-parotid fever must be regarded as a clinical variant of sarcoidosis.

If both parotid and lachrymal glands are enlarged a clinical picture resembling Mikulicz's syndrome is seen. Mikulicz in 1888 and again in 1892 described a "peculiar symmetrical disease of the lachrymal and salivary glands." There is no uniform ætiology for this syndrome and one of the possible ætiological agents is tuberculosis.

The hypophysis cerebri has been involved (Schaumann, 1936; Tilgren, 1935; Lesne, 1935). In such cases symptoms of diabetes insipidus have been found.

Individual cases are on record of infiltrations in many other sites: breast (Goeckermann, 1928); mucosæ of the upper air passages (Boeck, 1916;

Mylius, 1928); pharynx and larynx (Bloch, 1907); knee-joint (Burman and Mayer, 1936); nervous system (Reis and Rothfeld, 1931); intestine and mesenteric lymph nodes in cases of regional ileitis (Homans, 1937); endocardium, pancreas, testis, vertebral and femoral marrow (Nickerson, 1937); and skeletal muscle (Bergel and Scharff, 1933).

### Diagnosis

The diagnosis of Besnier-Boeck's disease is not always simple. The disease may be recognised not only by the cutaneous lesions but by manifestations elsewhere such as pulmonary, osseous or ocular changes, which may give rise to the presenting symptom.

The generalised nature of the process must be kept in mind and sarcoidosis should be considered whenever papulous, nodular, acneiform and chronic cutaneous lesions are met. Chronic chilblains, tenacious ocular lesions and unimproved lymph-adenopathy may also indicate the disease. True tuberculides, true chilblains, spina ventosa, miliary tuberculosis and Hodgkin's disease have to be excluded.

The affection is usually chronic, worse in winter than in the summer, and it is compatible with a fair state of general health. A tentative diagnosis may be made on a careful clinical and radiological examination. An exact diagnosis is only possible by biopsy and histological and bacteriological examination. A complete examination of the blood and estimation of the total serum proteins is of considerable help in certain cases. Schaumann (1934) attaches decided importance to the cutaneous reaction to tuberculin, which should here be negative. Inoculation of guinea-pigs with fragments of all forms of tissue or with blood from a case of sarcoidosis does not produce tuberculosis in the first generation.

The diagnosis of Besnier-Boeck's disease depends principally upon the clinical picture, the histology, the absence of bacilli, the radiological picture of the lungs and bones, and the anergic reaction to high concentrations of tuberculin.

The chief clinical evidences of the disease occur in the skin, and sarcoidosis must be differentiated particularly from leukæmia cutis, lymphadenoma cutis, leprosy, nodular lupus erythematosus, syphilis, various forms of tuberculosis cutis and the Darier-Roussy sarcoid.

Tuberculosis of the skin may show itself in various ways. True tuberculosis of the skin is of two types: In one form, the exogenous type, there is a direct implantation of the tubercle bacilli into the skin as exemplified by the anatomical tubercle or tuberculosis verrucosa cutis. In the other, the endogenous type, the infection is carried to the skin by the blood stream or by direct extension from some deeper tuberculous process in

bone, lymph gland or from excretions from the lung. Examples are lupus vulgaris and scrofulodermia. Another group, the tuberculides, associated with tuberculosis elsewhere in the body, have a distinct histology, and are considered to be due to toxic products of the infection or hypersensitivity to the same. Examples of this group are lichen scrofulosorum, acne scrofulosorum, papulo-necrotic tuberculide and erythema induratum (Bazin's disease).

The gummatous tuberculide or erythema induratum (Bazin's disease) is not uncommon and is fairly easily differentiated from the cutaneous sarcoids. The disease is almost entirely confined to the legs, especially the calves, and is usually bilateral. The initial lesion is a deep-seated nodule, from a pea to a hazel-nut in size, starting in the subcutaneous fat. The nodule slowly increases in size, involves the skin, which becomes purplish in colour, and eventually softens and ulceration occurs. These lesions are chronic and relapsing in character and the association with tuberculosis is definite.

Erythema nodosum is now often regarded as intimately related to tuberculosis, the lesions being toxic rather than areas of infection. If this is true erythema nodosum should be included in the group called "tuberculides" mentioned above. The isolation of the tubercle bacillus from the lesions originally reported has not been confirmed. Erythema nodosum is usually bilateral and confined to the lower limbs. It rarely recurs in the same patient and it does not leave a scar after the lesion heals. These points are sufficient to differentiate erythema nodosum from the cutaneous lesions of Besnier-Boeck's disease.

Darier and Roussy (1906) described an unusual, but not rare, nodular eruption which they differentiated from the sarcoid of Boeck because it affected the hypoderm, particularly the adipose tissue rather than the corium of the skin. The Darier-Roussy sarcoid chiefly occurs about the lower limbs, but may also be seen on the trunk. It commences as deep, rather painful nodules in the subcutaneous fat, which may eventually involve the skin, producing a localised redness. The nodules gradually enlarge to the size of a hazel nut, flatten out and become broad and hard. Several lesions may coalesce to form one large plaque. When the lesions subside some fibrous contraction may be present. The lesions are not usually very numerous. They never ulcerate, which distinguishes them from erythema induratum of Bazin, and they never metastasise to the bones or organs, which distinguishes them from the sarcoid of Besnier-Boeck.

The tuberculin test was found by Sulzberger and Wise (1931) to be negative in sarcoidosis more often than in normal people. In a comprehensive article on tuberculin, they found that 98 per cent. of normal

individuals had a positive reaction to a 1 : 5,000 dilution, and 50 per cent. were positive to a 1 : 1,000,000 dilution. In a group with sarcoid lesions 32 per cent. reacted positively to a 1 : 5,000 dilution, and only 11 per cent. to a 1 : 1,000,000 dilution. It has been noted that tuberculides in which tubercle bacilli are rarely or never found also exhibit this form of positive anergy.

The microscopic pathology in well-developed Darier-Roussy sarcoid is fairly characteristic inasmuch as the lesions are all confined to the hypoderm of the skin. They are sharply circumscribed tubercles, which are separated from one another by connective-tissue septa, composed of epithelioid cells, lymphocytes, and Langhans' giant cells. They seem to arise from perivascular tissue and there is seldom or never any evidence of necrosis or caseation. The changes in the epidermis are always secondary.

The enlarged lymph glands must be differentiated from tuberculous glands, leukæmias, Hodgkin's disease or malignant disease. A biopsy of a gland is necessary in all cases. The enlarged spleen may be mistaken for Banti's disease.

The X-ray pictures of the bone lesions may be simulated by many diseases—syphilis, leprosy, tuberculosis, gonorrhœa, and gout. If the characteristic blue-red discoloration of the skin of the fingers, fusiform swelling of the phalanges, and dystrophic changes of the nails is accompanied by enlargement of the spleen or lymph glands, a diagnosis of Besnier-Boeck's disease is justifiable from an examination of the skiagram.

When the lungs are involved a distinct help in the diagnosis of pulmonary sarcoid is the spectacular discrepancy between the massive anatomical involvement as shown by the X-ray, and the absence or paucity of respiratory or constitutional symptoms and the absence of physical signs.

The enlarged hilum glands must be differentiated from tuberculous glands, Hodgkin's disease and new growth. Diagnosis of pulmonary sarcoid from the radiogram alone is not possible. The most likely condition that the radiological picture may be mistaken for is miliary tuberculosis. The shadows are usually coarser and less regularly disposed in pulmonary sarcoid than in miliary tuberculosis of the lungs.

The diagnosis of pulmonary sarcoid can only be confirmed at necropsy and by histological examination of the lesions. But if associated lesions are available for biopsy such as skin or lymph nodes, and these show the characteristic histological picture, it is safe to assume that the pulmonary condition is due to the same cause. This can be done with increased confidence if a third lesion such as iridocyclitis exists or has occurred previously.

Syphilis is excluded by a negative serological examination. It should

be borne in mind that a positive Wassermann reaction may mean the presence of co-existent syphilis.

What histologic criteria are necessary to make the diagnosis of sarcoid and to differentiate it from tuberculosis? Nickerson (1937) in his report of six necropsies on patients with Besnier-Boeck's sarcoid gives the following description of the microscopic picture as typical of the condition:

"The lesions were well defined single or confluent round inflammatory lesions, consisting of fibrous tissue, infiltrated by moderate numbers of elliptic macrophages and a few lymphocytes. About the periphery were fairly numerous lymphocytes and occasional macrophages and eosinophilic polymorphonuclear leucocytes. Many of the lesions contained multinucleated giant cells. No areas of caseation were present, and only a rare neutrophilic polymorphonuclear leucocyte was noted. About the nodules there were wavy bundles of homogeneous eosinophilic material. With silver impregnation this was shown to be collagen, which appeared to result from condensation of reticulum about each nodule. This stain also showed the presence of a delicate network of reticulum in each nodule."

In differentiating sarcoid from tuberculosis, especially the miliary form, the following findings are of assistance: Caseation should never be present. In none of the lesions of sarcoid are any neutrophilic polymorphonuclear leucocytes seen, a finding one would expect in an early caseating tubercle. The giant cells are different from those seen in tuberculosis. They show moderate variation in size, are usually much larger and contain many more nuclei (often as many as from 25 to 30) which are evenly distributed throughout the cell and are seldom arranged in the elliptic manner typical of tuberculous giant cells.

Lesions in tissues other than the lungs do not contain carbon pigment. In the liver the lesions are most numerous in the portal triads, with only a few in the midzones of the lobules. In miliary tuberculosis the reverse is true. With silver impregnation, a delicate reticulum is always present in the lesion. In tuberculosis this is destroyed by the onset of the caseation. Finally, no evidence of tuberculosis is found anywhere in the body.

Many authors believe that giant cells should never be present in the older, quiescent lesions, as they assume that their presence denotes activity of the infection. Nickerson believes that giant cells may occur in all stages of the disease, and he states that the amount of collagen present seems to be a more accurate index of the activity of the infection, the presence of increased amounts of collagen indicating a healing reaction.

### Course, Prognosis and Treatment

Clinically, Besnier-Boeck's disease is an extremely chronic disease. It usually persists over a number of years and may cause only slight constitutional symptoms. A relapsing course is not uncommon, involving one organ or tissue of the body after another, and in some situations it may be recurrent.

The prognosis on the whole is favourable. The disseminated form of the disease may pursue a chronic and benign course. Spontaneous healing may take place and the changes in the lungs may disappear entirely, and moreover the bone lesions may also subside.

Many of the signs of the disease often disappear during observation of the case. Snapper (1938) has observed patients over a long period of years. One of his cases had in 1915 the following syndrome: bilateral iridocyclitis; skin lesions of the face and legs, proved to be Boeck's sarcoids by biopsy; considerable enlargement of liver and spleen; enlargement of peripheral lymph glands; benign sarcoids of soft palate and conjunctivæ; and a leucopenia. On re-examination in 1935, twenty years later, the general condition was excellent. The enlargement of the liver and spleen and lymph glands had disappeared completely. The eyesight was much impaired by the scars of the iridocyclitis. There were also small scars on the face where the sarcoids had been localised. A skiagram of the chest then showed some enlargement of the hilar glands. In the phalanges a few tiny cystic defects were found.

In another of his cases seen in 1930, a girl of fifteen exhibited the following features: X-ray of the lungs showed swelling of the hilar glands and extensive nodular dissemination in both lungs. These nodules had been coarser than the fine granules found in miliary tuberculosis. At the time a radiological diagnosis had been made of hæmatogenous or old miliary tuberculosis. Splenomegaly and swelling of several groups of lymph glands were also found. There was also a leucopenia with shift to the left and a high erythrocyte sedimentation rate. In 1930 the diagnosis of tuberculosis could not be proved. Biopsy of a swollen lymph gland had shown only nodules of epithelioid cells with some giant cells but without caseous necrosis and without tubercle bacilli. The patient was re-examined in 1935. The general condition was satisfactory. The general dissemination in the lungs had nearly disappeared. In 1937 the lungs had become completely normal again. It was evident that the diagnosis made in 1930 on the X-ray pictures of the lungs had been erroneous. Careful re-examination of the slides of the biopsy of 1930 proved the presence of multiple Boeck's sarcoids.

The treatment has been entirely empirical and in many instances the

disease has been found highly refractory to treatment. General hygienic and dietetic measures should be carried out. If the lungs are involved routine sanatorium treatment with bed rest and graduated exercise is of great value.

Arsenic in moderate or large doses has been employed by most observers. It is interesting to note that Boeck pointed out that the benign sarcoids of the skin react favourably to arsenic, while genuine tuberculosis of the skin is not influenced by the drug. Other drugs recommended are: large dose of vitamin C; chaulmoögra oil; subcutaneous injections of gold; Finsen rays, ultra-violet light, X-rays and radium have all been used in certain cases but with variable success. Tuberculin may be beneficial in cases of pulmonary involvement; but since the results of specific therapy have been uniformly unfavourable when the patient is anergic, it should only be attempted for those cases which react positively to a dilution of 1 : 1,000 or greater. Focal reactions should be avoided and the injection is repeated when the preceding reaction subsides completely. This occurs within two or three weeks, and treatment should be continued for some time after the entire resolution has been effected (Irgang, 1939).

When the mucous membranes are involved, intramuscular injections of " antileprol " (a preparation which is extracted in part from chaulmoögra oil) have been beneficial (Lomholt, 1937).

**Discussion.**

Besnier-Boeck's disease should be accorded wider recognition because it often occurs as a generalised process in which skin manifestations are frequent but not constant. Considerable interest is attached to its ætiology and the clinician is impressed by the widespread and protean nature of this bizarre condition.

The onset of the disease is usually insidious and the constitutional symptoms are slight even when the pathological changes have progressed to an extensive involvement of the lungs. Some writers have remarked that fever is usually high when the lungs are extensively diseased, but this feature is not common. Recently I had the opportunity of observing a case for nearly a year in which the nodular dissemination in the lungs was massive. The patient was afebrile for most of that time, fever of only slight degree being present for a week or so at the times of an outbreak of a fresh crop of cutaneous eruptions.

With a more thorough study of patients with sarcoidosis, abnormalities of the lungs will probably be found more frequently. The radiographic shadows are usually dense and extend from the roots of the lungs towards the bases principally.

The disease progresses slowly over a number of years and may affect

many organs. Pain and emaciation are usually absent, but a complaint of tiredness is frequent. Cough, expectoration and dyspnœa sometimes occur. If the larynx is affected hoarseness may be the presenting symptom. Jaundice has been noted and when it occurs it is frequently recurrent. Ocular symptoms are frequent and the patient is often first seen by the ophthalmologist. The disease may begin with an enlargement of the parotid glands and a diagnosis of mumps may be erroneously made. Enlargement of the lymph-nodes is constant. The lesions in the bones are almost specific, and they are usually present in the phalanges when the cutaneous lesions are present in the fingers and toes. The peripheral and central nervous system are rarely affected with sarcoidosis. Examination of the blood does not show any regular deviations from the normal as a rule. There is rarely anæmia, nor are there constant or characteristic changes in the numbers or proportions of leucocytes. Schaumann (1921) states that not much value can be attached to the finding of tubercle bacilli in the sputum of patients with sarcoidosis, since it is impossible to know in what phase of the disease the pulmonary lesions are. The sarcoid tubercle may be considered the extreme representative of the productive reaction in tuberculosis. As the productive reaction predominates in undoubted tuberculous foci, it is increasingly difficult to demonstrate the tubercle bacillus.

The ætiology of Besnier-Boeck's disease has been the subject of much controversy. Many authorities believe that the tubercle bacillus or some product of its growth is the causative agent. Dermatologists frequently state that they consider the condition a non-specific tissue response which may be evoked by many pathogenic agents. English authorities have a tendency to believe that sarcoidosis holds a position somewhat analogous to Hodgkin's disease. Because of the changes in the bones some writers believe that the condition is closely related to leprosy, and Murdoch and Hutter (1932) state that the marbled appearance of the lungs which is considered pathognomonic for pulmonary sarcoidosis, is often found in leprosy. It is generally agreed that the condition is not syphilitic. The most likely explanation of the cause of the disease is that it is a chronic infectious granuloma due to a virus infection and probably a separate pathologic entity. Probably the most important evidence in this connection is the uniform histology of the lesions.

The relationship of trauma to sarcoidosis has been stressed by several writers. Maloney and Combes (1936) have reported a case in which sarcoid lesions appeared at the sites of hypodermic injections, and one case involving a finger which had been previously injured. Ernsting (1937) reports a case in which Boeck's sarcoid appeared in the scar of an eyelid which had been injured fifteen years before. Montanus (1938) reports a

case of sarcoid occurring in an appendicectomy scar four years after the operation was performed.

The question of mutation of the tubercle bacillus must receive serious consideration with reference to sarcoidosis. The investigations of Beinhauer and Mellon (1938) have added renewed incentive to the study of the relation of non-virulent non-acid-fast forms of this micro-organism to this disease. The lowering of tissue resistance may account for their reversion to the virulent-acid-fast state, thus explaining why sarcoid may in a small fraction of cases result in a progressive caseous tuberculosis and terminate fatally as pulmonary tuberculosis, Addison's disease, tuberculous meningitis, or renal tuberculosis. The theory of mutation may explain the rare instances of fatal termination in sarcoidosis.

One of the principal reasons why this condition has been for so long overlooked or unrecognised by the clinician is probably because of its confusing nomenclature. As long as the ætiology remains obscure and as long as diseases are eponymously designated it is historically justifiable to describe the syndrome as Besnier-Boeck's disease. Besnier was the first to give an elaborate account of the condition which he called " lupus pernio," and Boeck fully described the clinical picture and microscopical structure of a characteristic skin affection which he called " multiple benign sarcoids of the skin." Boeck also appreciated the importance of the visceral lesions of the sarcoids.

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# CASE REPORT

From the Clinical Department of King George V. Jubilee Hospital for Tuberculosis, Durban.

By B. A. DORMER,
M.D., D.P.H. B.HY.,
AND
J. FRIEDLANDER,
M.B., CH.B., D.P.H.

V. P., native female, married, aged thirty-three, housewife.

*Complaint.*—Cough and expectoration of two months' duration.

*Previous History.*—No preceding chest trouble. No history of any skin affection. Operated on for "tumour of neck" about five-six years ago (no record available).

*Family History.*—Husband and child quite well—no skin lesions. No cough. No complaint of cough amongst immediate neighbours.

*History.*—Patient lived in a mission reserve, doing her own housework. She insisted that she felt quite well and was able to do her work prior to two months ago. She then developed a non-productive dry cough. About a month later some sputum, mucopurulent in nature, appeared. The amount of sputum has greatly increased during the last three to four weeks and her condition has retrogressed rapidly. She was admitted to hospital about three weeks ago, and in hospital had a slight hæmoptysis on one occasion. No history of night sweats. There was loss of appetite. Rapidly increasing dyspnœa during last two weeks or so.

On examination (when first seen at the King George V Jubilee Hospital for Tuberculosis):

*General.*—Patient was a well-covered native female. There was marked orthopnœa, cough and profuse mucopurulent nummular-looking sputum. Tongue furred. Mucous membranes showed good colour. No clubbing of fingers. No adenopathy. Skin smooth and resilient, with no evidence of previous dermatitis. Thin scar at base of neck in front.

*Respiratory System.*—Orthopnœa.

*Lungs.*—Physical signs in chest were those of a bilateral fairly advanced case of pulmonary tuberculosis, with dullness, crepitations, amphoric breath sounds, etc.

*Sputum: Direct Smear.*—T.B. negative; pus cells. *On Concentration.*—T.B. negative. *Hæmalum-Eosin stain for Malignant Cells (Dudgeon's Technique).*—Negative. *Culture on Lowenstein-Jensen Medium.*—Moulds and secondary

# PLATE XIV

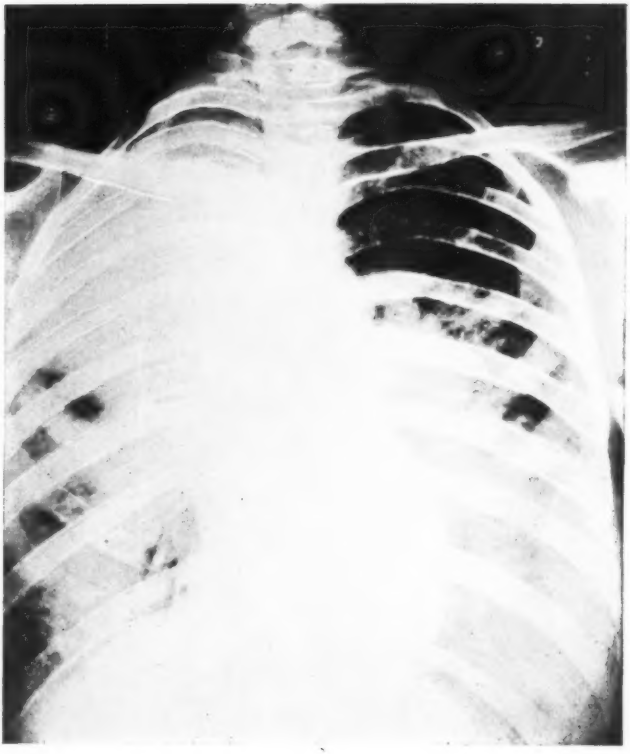

FIG. 1.

[*To face page* 114.

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# PLATE XV

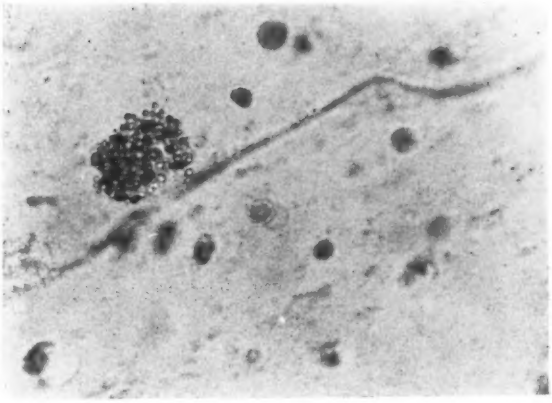

FIG. 2.

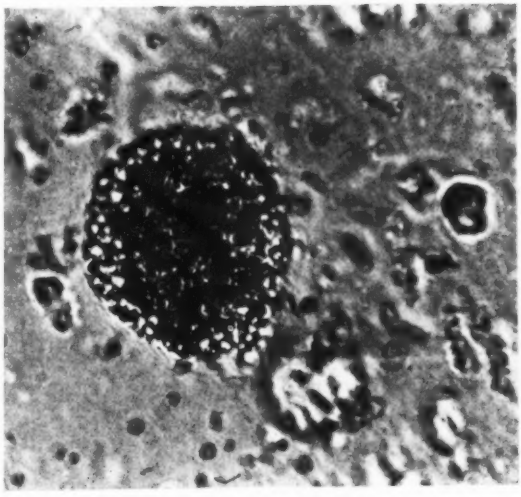

FIG. 3.

[*To follow Plate* XIV.

organisms. Nil else. *Unstained Films.*—In every specimen examined large round bodies were seen—circular bodies containing multiple spores surrounded by a thin membrane not definitely doubly refractile. There was variation in the size of these bodies. Many of these bodies were seen with surrounding membrane ruptured and spores lying free. These bodies were persistently found in all the specimens of sputum examined (see microphoto).

*Blood Examination : Total R.B.C. Count.*—5,130,000.

*Hb. per cent. (Dare).*—109 (=17·6 gms. per cent.).

*W.B.C. : Total.*—13,500.

*Diff.*—Polys. 73; Lymph. 25; Monos. 2; Eosin. —.

*Von Bonsdorff Index.*—0·68.

*B.S.R. (Cutler).*—22 mm. (1 hour).

*X-ray.*—General appearance not unlike a miliary tuberculous spread with pneumonic consolidation right upper lobe.

*Discussion.*—Clinically and radiologically the patient showed the evidences of a rapidly advancing bilateral tuberculosis. In view of the repeatedly negative sputa for Koch's bacilli, we began to doubt the clinical diagnosis of tuberculosis, and began to search for another etiology. Before sputum was collected, the patient was made to rinse her mouth out well with 50 per cent. alcohol to remove any oral flora that might contaminate the sputum. In every specimen the round bodies described were seen, and no other etiological agent could be found. Could this be a case of fungus infection due to *Coccidioides immitis* or other similar related group?

After examination at the King George V Hospital for Tuberculosis, the patient went back to the hospital where she was being treated, and left soon after. She died outside, and as efforts to locate her failed no post-mortem was done.

Our prime reason for publishing this case, incomplete as it is, is to draw attention to the possibility of fungoid chest conditions in this country.

## REFERENCES.

California Department of Public Health, Special Bulletin, No. 57.

Farness and Mills : *Amer. Rev. of Tub.*, vol. xxxix., No. 2, February, 1939.

Dickson and Gifford: "Coccidioides Infection" (*Arch. of Int. Med.*, vol. lxii., No. 5, 1938).

# MEETINGS OF SOCIETIES

## JOINT TUBERCULOSIS COUNCIL

A MEETING of the Joint Tuberculosis Council was held at the London School of Hygiene and Tropical Medicine on Saturday, March 1, 1941.

There was a good attendance of members. It was decided that the next meeting of the Council should be held in London if possible on Saturday, May 17, 1941. The Honorary Secretary (Dr. J. B. McDougall) reported that there had been a good response to the enquiries addressed to Deans of Medical Schools with reference to the teaching of students in tuberculosis during war-time. Most schools had made arrangements directly or indirectly with local authorities for students to attend tuberculosis dispensaries or sanatoria in the near neighbourhood of their temporary residence.

The following officers were appointed for 1941:

*Chairman :* Dr. D. A. Powell.
*Vice-Chairmen :* Drs. James Watt and Ernest Powell.
*Honorary Auditor :* Dr. D. P. Sutherland.
*Honorary Treasurer :* Dr. G. Jessel.
*Honorary Secretary :* Dr. J. B. McDougall.

The Hon. Treasurer gave his annual statement of the accounts of the Council and reported a balance in hand of over £80.

" The Co-ordination of Tuberculosis Services of Local Authorities " was introduced by Dr. G. Lissant Cox in a memorandum which had been circulated previously to the Council. Amongst the most important points in the memorandum were the following.

### ENGLAND.

1. Many local authorities are not large enough to deal adequately with prevention and treatment of tuberculosis on modern lines. Some form of combination or regionalisation is required throughout England and Scotland. It already exists in Wales.

2. It will be appreciated that the special problem in any tuberculosis scheme is the combination of prevention and treatment; and any scheme which does not provide full and proper combination of means for prevention as well as for treatment is a bad scheme.

3. *Prevention* of tuberculosis in England is undertaken by the county boroughs, non-county boroughs, urban districts and rural districts (but not

by counties as such), under the Public Health (Tuberculosis) Regulations, 1930, with roots in the 1875 and 1896 Public Health Acts.

4. *Treatment* of tuberculosis is the responsibility of the counties and county boroughs and originated in compulsory form from the National Insurance Act of 1911, the Public Health (Tuberculosis) Act of 1921 and consolidated in the Public Health Act of 1936. The obligation is definite and clear, as the exact wording shows:

Public Health Act, 1936. Sec. 171. (1) It shall be the duty of the council of every county and county borough to make adequate arrangements for the treatment of persons in their county or borough who are suffering from tuberculosis, at or in dispensaries, sanatoria, and other institutions approved by the Minister.

5. The councils of counties and county boroughs responsible for the organisation of tuberculosis schemes in England deal with populations varying from under 50,000 to 2,000,000 (excepting London); and the counties vary considerably in geographical area. Although these authorities are supposed to have schemes similar in efficiency and completeness, in practice it is found that this is not the case. It is well known, also, that the schemes of similar local authorities vary on account of the calibre and vision of the authority and the staff they employ. But for so complicated and expensive a public health work as a complete anti-tuberculosis scheme, a large authority is in a position to provide more economically a modern scheme than a small and poor authority.

6 There are some relatively small counties and county boroughs with schemes whose efficiency is not low, but they are usually fortunate in having a person of exceptional ability to direct the scheme, or having in the area peculiar advantages.

7. Many of the smaller authorities would have the efficiency of their schemes improved if they combined one with another or with the county area adjoining. There is ample legislation to enable local authorities, if they wish, to combine and form joint committees or joint boards for the purpose of carrying out their statutory duties in regard to tuberculosis. But joint committees or joint boards dealing with tuberculosis on a wider scale than an individual authority are rare in England. There are only three: (1) Staffordshire, Wolverhampton, and Dudley Joint Board for Tuberculosis; (2) Gloucestershire Joint Board for Tuberculosis; and (3) Warwickshire and Coventry Joint Committee for Tuberculosis. The action of these local authorities in combining has resulted in the setting up of three efficient schemes for the prevention and treatment of tuberculosis; and there is more co-operation between the institutional side and the

dispensary side and more team work than in many of the individual county or county borough schemes.

8. It is possible, by agreement, for a small authority to have its tuberculosis work done by a larger authority. An example of this is the small county borough of Canterbury, which has its tuberculosis work done by the Kent County Council.

9. The Joint Tuberculosis Council in 1932 recommended that rural areas of 200,000 and urban areas of 300,000 could be managed by one whole-time tuberculosis officer with adequate medical and clerical assistance. They also recommended that a small area should form with an adjacent area a joint committee to administer the tuberculosis scheme, or alternatively that a small area should allow its work to be done, under agreement, by a larger authority.

10. Areas adequate for some aspects of tuberculosis work, for example isolation, nursing, and some minor surgical treatment, can be smaller than areas for more specialised treatment. Thus, treatment for non-pulmonary disease (especially bones and joints) for children and *adults* can only be dealt with efficiently and economically by large areas (or combinations of small areas) and the institutions should be large. Major thoracic surgical work requires similar arrangements. Every tuberculous patient should have the opportunity to receive modern treatment.

11. As is indicated in 7 above, local authorities are unwilling to surrender any of their powers under the Public Health Acts. Legislation should be enacted to enforce the combination of authorities too small to provide efficient schemes.

## Wales.

12. In Wales and Monmouthshire the diagnosis and treatment of tuberculosis are most efficiently conducted by the Welsh National Memorial Association. This Association is in reality a combination of the thirteen counties and four county boroughs in Wales for tuberculosis purposes. It is a regional scheme on a big scale. But in the matter of prevention the Association scheme is weak. We know from the report of the Committee of Inquiry into Anti-Tuberculosis Services in Wales and Monmouthshire that the responsibilities of local authorities in the matter of prevention have not been properly realised, and their duties and those of many of the part-time medical officers of health have been neglected. This again is an argument for larger local authorities, for a prime cause of the neglect has been the small size and inadequate financial resources of these bodies. The very excellence of the Memorial Association scheme on the diagnosis and treatment side seems to have been an excuse for neglect on the preventive side.

### Scotland.

13. The prevention and treatment of tuberculosis in Scotland are governed by the law of general infectious diseases, and it would appear that general powers should be conferred on the Scottish authorities similar to those in England.

14. There are special geographical difficulties in many parts of Scotland, and for the purpose of diagnosis clinics would appear to be the best solution.

15. The administrative areas are smaller in population than in England, and these small independent authorities in nearly every case have a medical officer of health who is also the clinical tuberculosis officer. This for the purpose of diagnosis is a bad arrangement, and is one of the many reasons for the necessity of reorganisation and regionalisation in Scotland.

16. A very good example of successful and efficient regionalisation is the Aberdeen Regional Scheme.

### British Hospitals Association.

17. An example of regionalisation is provided by the scheme of the British Hospitals Association. For many years this Association has had an organisation by which the country is divided into 23 regions, one of which covers the whole of Scotland. The regions have committees and honorary secretaries, and hold meetings for the discussion of hospital matters in their areas, and there is a central council which meets in London. As the result of a Commission which reported on voluntary hospital matters in 1937, the Association have now provisionally agreed upon the division of England and Wales into 14 regions for their purposes. It may be well that the tendency is not so much to increase the size of the areas as to decrease the number of regional bodies, as it was stated in the Commission's report that 5 of the 23 regions were " to all intents and purposes inactive."

### Emergency Hospital Scheme and Regionalisation of Ministry of Health.

18. There are two recent examples of regionalisation in the country for health and war purposes. One is the Emergency Hospital Scheme of the Emergency Medical Service, and the other is decentralisation of a large part of the staff of the Ministry of Health.

19. In 1938 the Ministry of Health organised a hospital scheme for air-raid casualties. For this purpose the whole country was divided into 12 regions, one of which covered the whole of Scotland, and another the whole of Wales.

20. On the outbreak of war, also, the Ministry of Health, for its long

contemplated decentralisation, adopted the same regions as in the Emergency Hospital Scheme.

21. The Emergency Medical Service regions—12 for Great Britain—do not lend themselves for tuberculosis areas for various reasons. Many contain part only of one county or parts of several counties. Unless county councils were abolished, anti-tuberculosis measures based on these regions, with present-day legal and other arrangements, would be more confounded than ever.

22. Except perhaps one, the regions are too big for basic tuberculosis purposes—*i.e.*, domiciliary supervision, dispensary diagnosis and treatment, isolation and treatment of most of the pulmonary cases.

23. Some of the regions, if the county boundaries were ignored, might be useful for certain hospital purposes—*i.e.*, treatment of non-pulmonary disease, major chest surgery, and perhaps rehabilitation schemes; but three of them would have to be divided for these purposes.

24. It is possible, however, that in spite of the difficulties described above, grouping of authorities in some regional areas might be made.

The two main conclusions arrived at were:

1. While the efficiency of prevention and treatment of tuberculosis is related to sizes of areas, population and rateable value, it depends even more on the concept of anti-tuberculosis work and the personnel who carry out the work. Many of the small authorities, however, do fall short of the high standard attained by some of the large authorities. If it were not for the fact that some of the small areas already combine in an unorganised way for part or parts of prevention, diagnosis and treatment, the general efficiency of their work would be lower than at present.

2. The best way to improve the efficiency and economy of the tuberculosis schemes of the small counties and county boroughs is to aim at regionalisation but not necessarily regionalisation on the exact lines of the Emergency Medical Service. The Ministry of Health, when making their "survey" reports on the public health services in an area, should bear closely in mind whether the tuberculosis scheme would not be more effective if merged into a much larger administrative unit. Legislation will be required to enforce a combination of local authorities held to be too small to provide efficient schemes.

An important report prepared by Dr. G. Jessel on Mass Radiology was considered by the Council, and it was decided that the offer of the Editor of the *British Journal of Radiology* for the publication of the report be accepted and that reprints be obtained and circulated to tuberculosis officers and others interested in the subject.

*Tuberculosis in War-time.*—In the unavoidable absence of the Convenor of the Committee (Dr. James Watt) the Council considered a memorandum prepared by Dr. F. R. G. Heaf on "Tuberculosis in Shelters." It was resolved that in view of the urgency of the subject the memorandum be sent to the Standing Advisory Committee and to the Society of Medical Officers of Health.

RECOMMENDATIONS BY DR. F. R. G. HEAF AND ACCEPTED BY THE COUNCIL AS FOLLOWS.

(1) That the tuberculous person shall not lack adequate air-raid protection because of the nature of his disability.

(2) That the healthy person frequenting public shelters shall not thereby incur greater risk of contracting tuberculosis than in normal life.

(3) That the recommendations of the Horder Committee be carried out as soon as possible.

(4) That the provision of special shelter accommodation for the tuberculous in densely populated areas be encouraged.

(5) That extra accommodation be provided for segregation of the open cases not needing treatment in hostels or in industrial settlements, the distinction between treatment and segregation being thus emphasised.

(6) That the present educational campaign be extended and anti-tuberculosis propaganda be given more attention by official bodies.

(7) That a special effort be made to examine more frequently contacts of known tuberculous cases using Anderson shelters and that such contacts be assured of adequate nourishment.

(8) That all children be removed from Anderson shelters used by tuberculous persons.

(9) That no tuberculous person be allowed to use a school shelter.

(10) That individuals using public shelters and presenting symptoms of pulmonary tuberculosis be persuaded to undergo an X-ray examination.

(11) That compulsory powers should be available if persuasion fails.

(12) That every effort be made to prevent the spread of catarrhal infections.

(13) That spitting be vigorously suppressed.

(14) The presence or history of tubercular disease must not be used as a means of gaining privileges which have no relation to the problem of preventing spread of infection and thereby allowing people to obtain special advantages over their fellows.

Many of these recommendations can only be applied during periods of comparative quiet. When bombing is intense little can be done in

segregating the tuberculous. It is therefore essential that action is taken whilst it is possible to enforce regulations so that a certain adherence to order and routine may be expected in times of extreme emergency.

Various items such as the shortage of nurses in sanatoria, reorganisation of Council committees and alterations in the constitution of the Council were delayed until the next meeting.

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## REVIEWS OF NEW BOOKS

*Tomography.* By J. B. McDougall, M.D., F.R.C.P.E., Medical Director, Preston Hall, Maidstone. London: H. K. Lewis and Co., 1940. Pp. 72. Plates 110. Price 21s.

This small volume is essentially an atlas of tomography in the normal subject and those affected by pulmonary tuberculosis. There are a few plates dealing with other branches of the subject, but the bulk of the work is concentrated on the sphere in which the author's own experience lies. The book is well produced, and the numerous plates are well chosen to show the part which tomography can play in the recognition of cavities.

*Man's Greatest Victory over Tuberculosis.* By J. Arthur Myers, Ph.D., M.D., F.A.C.P. Pp. 419. 31 illustrations, including plates. Price 27s. 6d. Published by Charles C. Thomas, Springfield, Illinois.

This is a curious book, a remarkable mixture of scientific fact, partial but detailed historical biography, veterinary medicine, dry records of the progress made in the State control of tuberculosis among cattle in the United States, and a final chapter, on the lessons to be learnt by physicians from a study of the practice of veterinarians, that reads very much like a cautionary tale. With such a mixture it is at times difficult to follow the thread of the author's account, but of his main theme there is no doubt. He traces, with all the enthusiasm of the zealot, the history of the prevention of tuberculosis in cattle, gives in detail the results achieved in America, and draws the conclusion that in this respect, prevention of the disease, veterinary medicine is forty years ahead of the medical profession.

As readers may have gathered, the trouble with this book is that it takes the evidence for a good case and overstates it. This is a pity, for of course there is firm truth in a good deal of what the author says, and his obvious enthusiasm to be rid of tuberculosis rouses admiration. He traces admirably the long campaign that has done so much to rid cattle of the disease in his own country, but to carry deductions to the field of human tuberculosis from this work is plainly not going to take us very far. The chief value of the book will probably be that it is a detailed guide to the veterinary aspects of the problem of prevention in America, and as such it may well retain a permanent place in the literature.

*An X-ray Atlas of Silicosis.* By ARTHUR J. AMOR, M.D. (Lond.), M.Sc. (Wales), 1941. Bristol: John Wright and Sons, Ltd. Price 30s.

This excellent monograph is a timely one in the literature of its subject. The importance of the pneumonoconioses increases, and coming from one with wide experience, as this atlas does, a collection of representative radiographs presented together provides a valuable addition to our standard records.

The plates are well produced, with short case histories in both English and French. Every type of silicotic lesion is pictured, and a few others of conditions which enter into the differential diagnosis. There is in addition a short account of the pneumonoconioses by way of prelude.

*Brompton Hospital Reports.* 1940. Volume IX. Pp. 175. Published by the Research Department of the Brompton Hospital. Price 5s.

The most recent volume of the Brompton Hospital Reports (Volume IX., 1940) consists of a collection of articles relating to chest diseases by the various members of the hospital staff. Many have been published in other journals or periodicals, though some are appearing for the first time.

The article by Roberts on " War Injuries of the Chest " gives an outline of the approach to traumatic chest surgery and the general principles of treatment involved. One point not emphasised sufficiently is the necessity of taking good antero-posterior and lateral X-ray films as soon as possible after admission and always before any operative procedure is undertaken. Physical signs in the acute traumatic chest are notoriously misleading. and patients are rarely ill enough to prevent taking an X-ray with a portable machine.

Price Thomas, on " Late Effects of Penetrating Injuries of the Chest," has drawn from his extensive experience of those wounded in the last war and only now exhibiting the effects of their old injuries. His explanation of the ætiology of these late effects stresses the importance of early and proper treatment of hæmothorax, empyema and retained foreign bodies in an attempt to reduce the incidence of these very disabling late effects.

Scadding, in an article on the " Diagnosis of Pulmonary Tuberculosis without Bacterial Confirmation," gives a remarkably clear account of the present position regarding this problem. He emphasises the types of tuberculous lesions in the lungs which one would not expect to produce tubercle bacilli in the sputum and proceeds to give an account of the various diseases which might simulate pulmonary tuberculosis, paying special attention to the group of chronic pneumonias, which at the present time appear to be common.

In an article on " Primary Carcinoma of the Lung " Roberts points out that the surgical treatment will only become more successful as diagnosis is made at a much earlier stage in the course of the disease. He emphasises the earliest symptoms, especially a " persistent dry cough appearing for the first time in a person at or above middle age who is otherwise well." In such patients he considers it is folly to wait for physical signs or X-ray changes to appear and advocates that every case should be bronchoscoped

without delay; only by so doing can the condition be recognised sufficiently early for treatment to be successful.

Gosse and Pollock, in an article on "Treatment by Phrenic Paralysis," have reviewed some forty cases so treated over a two-year period. Unfortunately their follow-up notes are not complete, and in some cases their results are based on communications alone without clinical and adequate X-ray examination. Without attempting any statistical survey they list a small series of patients in whom phrenic paralysis was used as a primary treatment of choice, and they believe that immediate results compare favourably with other methods.

Livingstone's short article on the "Termination of Artificial Pneumothoraces" is full of sound advice. He stresses the importance of obtaining a satisfactory and efficient artificial pneumothorax. Division of adhesions either through the thoracoscope or by open thoracotomy has assumed a place of prime importance, though the latter procedure is losing popularity now owing to the high incidence of following purulent effusions—often some considerable time after the operation.

Brooks, Jules and Williams report forty cases of chronic recurrent iridocyclitis of indefinite ætiology which they have investigated from the point of view of a tuberculous background. They conclude that the majority of these are tuberculous in origin though the pathogenesis is a matter of uncertainty. They show the value of adequate bed rest followed by a sanatorium regime, and also report beneficial results from X-ray therapy in those cases presenting enlarged lymph glands.

This volume of the reports maintains the excellent standards of its immediate predecessors and provides interesting and instructive reading.

THE TUBERCULOSIS BUREAU OF THE HEALTH DEPARTMENT

WRIGHT'S PUBLICATIONS

INDEX OF DIFFERENTIAL DIAGNOSIS OF MAIN SYMPTOMS

INDEX OF TREATMENT

Three Excellent Books

- GYNAECOLOGICAL AND OBSTETRICAL TUBERCULOSIS. By Edwin Klebs, M.D., F.R.C.P. (Edin.). 10s. net.
- TUBERCULOSIS: BACTERIOLOGY, PATHOLOGY AND LABORATORY DIAGNOSIS. With Sections on Immunology, Differential Diagnosis and Bacteriophagy. By E. R. Baldwin, M.D., S. A. Petroff, M.D., and I. S. Gardner, M.D.
- INTESTINAL TUBERCULOSIS: Its Pathology, Diagnosis and Differentiation, and Its Secondary Obstructive Lesions. By Lewis Jones, M.D., F.R.C.S. (Edin.). Second Edition. Revised and Enlarged. 7s. 6d. net.

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